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SCHISTOSOMIASIS OF THE CENTRAL NERVOUS SYSTEM

Experiences in World War II and a Review of the Literature

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INVASION of the central nervous system is a rare complication of human schistosomiasis. The literature dealing with the various clinical manifestations of this disease is extensive, but only a few reports record associated abnormalities of the central nervous system. Recent large scale military operations on the island of Leyte in the Philippines have served to focus our attention on schistosomiasis japonica and, in addition, have presented an unusual opportunity to observe a significant number of cases with these complications. It is important to recognize the possibility that additional cases with involvement of the central nervous system may occur in occupation troops in endemic areas. This possibility should be kept in mind not only with respect to men who present the usual clinical features of the disease, but in all cases of persons who have been exposed to the infection. Furthermore, continued vigilance is necessary, since manifestations referable to the central nervous system with onset as long as two to four years after initial infection may be the presenting symptoms of the disease in some cases.

No attempt will be made here to describe in detail the clinical syndromes which follow infection with each of the three schistosomes found in men (Schistosoma japonicum, Schistosoma mansoni and Schistosoma hematobium). However, before we review the literature on complications involving the central nervous system of schistosomiasis in general, it may be advisable to outline briefly certain salient features of human Asiatic schistosomiasis, or "Katayama disease," due to S. japonicum, which was the organism involved in the cases to be reported in this paper.

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Geographically, schistosomiasis japonica is restricted to the Orient, and no case is known in which the disease has been contracted outside the endemic areas in China; Japan; Formosa; the Philippine Islands of Leyte, Samar, Mindoro and Mindanao; Celebes, and, possibly, upper Burma, near the Chinese border.

In our opinion, the best description of the usual mode of development of the disease in the mammalian host is that contained in Faust and Meleney's monograph, published in 1924.[1] While open to some criticism, their scheme of dividing the disease process into three stages is a useful one.

After exposure to contaminated fresh water for even a few minutes, the skin is penetrated by the microscopic, fork-tailed cercariae, which have previously undergone development in certain species of fresh water snails, and the first stage of invasion has begun. This stage lasts approximately one month in man. During this period the young parasites (of separate sexes) eventually find their way into the venules of the superior mesenteric vessels. Animal experiments offer proof that the main course followed from lungs to liver during this migration is via the pulmonary veins and not by direct penetration of the diaphragm, as was once believed. No multiplication of the parasites occurs within the hepatic portal system, and the adults rarely cause a reaction in situ. After mating, the second stage of deposition and extrusion of eggs begins and, in the absence of effective treatment, may go on for perhaps ten to twenty years. After an interval, which is usually four to six weeks from the date of the first exposure, the ova either begin to be extruded through the intestinal mucosa into the lumen of the bowel, and so appear in the stools, or are carried by tributaries of the hepatic portal system to the liver. The great egg-laying tendency of the female of S. japonicum, which may deposit hundreds of ova daily, has an important bearing on the seriousness of infection with this parasite. The third stage, which is said to come on in three to five years, consists in extensive proliferation of tissue and in attempts by the host to repair hepatic, intestinal and other damage caused by the repeated influx of ova acting as foreign bodies.

The classic clinical course parallels closely the pathologic course. The first stage (four to six weeks) may or may not be initiated by generalized cercarial dermatitis. There is an insidious onset of fever, malaise, anorexia, progressive loss of weight, urticaria or angioneurotic edema, cough and various abdominal complaints, and the blood shows leukocytosis with intense eosinophilia. Although the beginning of the second stage is often indistinguishable from the end of the first, clinically it is usually characterized by epigastric or upper abdominal cramps,

1. Faust, E. C., and Meleney, H. E.: Studies on Schistosomiasis Japonica, Monographic Series no. 3, Baltimore, American Journal of Hygiene. 1924.

continued fever and malaise, the presence of blood and mucus in the stools—with or without diarrhea—gradual enlargement of the liver and later of the spleen and the presence of the characteristic ova in specimens of stools. Although no cases in American military personnel have, so far as is known, progressed to the third stage, this phase of the illness is well recognized in natives of endemic areas. It is characterized chiefly by the insidious onset of symptoms of portal obstruction and hepatic cirrhosis and may go on to a picture indistinguishable from that of Banti's syndrome (splenomegaly). Carcinoma of the intestine is not a rare complication of the untreated disease.

It is with the unusual phenomenon of localization of ova beyond the confines of the hepatic portal system, in the brain and the spinal cord, that we are concerned in this report.

REVIEW OF THE LITERATURE

Period I (1889-1944).—Twenty-four cases of cerebral complications due to infection with schistosomes were reported prior to World War II. Of these, S. japonicum was involved in 14 cases.

Although he was not fully aware of the significance of his discovery at the start, it was a Japanese investigator, Yamagiwa,[2] who, in 1889, first attributed pathologic changes in the human cerebral cortex to the deposition of parasitic ova. He originally identified these ova as those of Paragonimus westermani, a common lung fluke of certain areas in the Orient. Later study of his sections, however, established their identity as the ova of S. japonicum.

In 1905, two other Japanese, Tsunoda and Shimamura,[3] demonstrated ova of S. japonicum in the brain of a man aged 37 who had jacksonian epilepsy and right hemiplegia. No adult worms were observed in the brain, but ova were seen in sections of the cortex, basal ganglia and internal capsule on the left. The spinal cord was normal.

Houghton,[4] in 1910, confirmed these observations in another case in which complications referable to the central nervous system were a prominent feature of proved infection with S. japonicum.

Ferguson[5] made a brief reference in 1913 to the observation of ova of S. haematobium in widely scattered areas of the brain and spinal

2. Yamagiwa, K.: Beitrag zur Aetiologie der Jackson'schen Epilepsie, Virchows Arch. f. path. Anat. **119**:449-460, 1890; cited by Faust and Meleney.[1]

3. Tsunoda, T., and Shimamura, S.: Beiträge zur pathologischen Anatomie der sogenannten "Katayama-Krankheit" zur Aetiologie der Hirngefassembolie und der Jackson'schen Epilepsie, Wien. med. Wchnschr. **56**:1681-1685, 1905.

4. Houghton, H. S.: Notes on Infection with Schistosomum Japonicum, J. Trop. Med. **13**:185-187, 1910.

5. Ferguson, A. R.: The Lesions of Bilharzial Disease, Glasgow M. J. **79**:14-23, 1913.

cord in 1 case of a series of 600 cases of the infection. The ova were identified by a maceration technic involving digestion in a 3 to 5 per cent solution of potassium hydroxide U. S. P. and subsequent sedimentation.

In the next report, appearing in 1930, Müller and Stender [6] recorded a case of complete thoracolumbar transverse myelitis in a man aged 26 who had traveled in southern Brazil. Death occurred six months after onset of the disease. Gross examination of the spinal cord showed thickening of the medulla in the thoracolumbar region with areas of poorly delimited, reddish gray softening. Scrapings from these areas contained large numbers of oval bodies with lateral spines, easily identified as ova of S. mansoni.

Chu,[7] in 1931, reported 1 case of jacksonian epilepsy and 1 case of right hemiparesis in a series of 39 Chinese patients with schistosomiasis japonica. Shimidzu,[8] in 1935, presented the case of an 18 year old male student with lower left and right quadrantic hemianopsia and bilateral papilledema, which came on six to eight months after exposure to schistosome-infected water in Japan. About one year after the initial exposure, a craniotomy was done and a firm (cystic) mass removed from deep in the posterior occipital region. The mass weighed 40 Gm. and on palpation appeared rough, "suggestive of sand." Microscopic examination showed many parasitic eggs the form, structure and size of which identified them as those of S. japonicum. The surrounding ganglion cells showed severe degenerative changes. All the arteries examined were normal, but the cerebral veins in the region showed phlebitic changes. Although the adult female was not identified in the extirpated portion of the brain, the author concluded that the eggs had reached the brain by direct deposition rather than by embolization. Two days after the operation the headaches disappeared, and three days after operation the hemihypesthesia also disappeared. Three weeks after operation the defects in the visual fields were still present, almost unchanged. Nine months after operation the patient was "able to work and had no subjective disturbances."

Nieva,[9] in 1935, reported a case from Samar, in the Philippines, in which the patient complained of generalized numbness, dizziness and

6. Müller, H. R., and Stender, A.: Bilharziose des Rückenmarkes unter dem Bilde einer Myelitis dorso-lumbalis transversa completa, Arch. f. Schiffs- u. Tropen-Hyg. **34**:527-538, 1930.

7. Chu, C. F.: Schistosomiasis Japonica in Nanking, Chinese M. J. **52**:651-664, 1931.

8. Shimidzu, K.: An Operated Case of Schistosomiasis Cerebri, Arch. f. klin. Chir. **182**:401-404, 1935.

9. Nieva, D. E.: Epileptiform Convulsions Probably Due to Schistosomiasis, Bull. San Juan de Dios Hosp., 1935, vol. 9, no. 7; cited by Vitug, Cruz and Bautista.[18]

headache and had epileptiform convulsions. Ova of S. japonicum were observed in the stools. The diagnosis was made in retrospect when the patient's condition improved dramatically after specific treatment with antimony potassium tartrate U. S. P. and emetine hydrochloride U. S. P.

Africa and Sta. Cruz[10] mentioned the presence of ova of S. japonicum in the brain in a case without symptoms referable to the central nervous system. Eggs were observed in the myocardium in greater abundance than in the brain.

Day and Kenawy,[11] in 1936, presented the case history of a 10 year old boy with transverse myelitis and complete flaccid paraplegia whose condition was originally diagnosed as anterior poliomyelitis. Serial sections of the spinal cord at the lumbar enlargement revealed minute necrotic areas which, on microscopic examination, were clearly seen to be due to noncalcified ova of S. haematobium. In addition, the surrounding nerve cells showed dissolution of the Nissl granules. The brain was normal, and no pathologic condition was noted in the genitourinary or the gastrointestinal tract.

An interesting and instructive clinical report is that of Egan's.[12] He described an outbreak of schistosomiasis japonica affecting two thirds of the complement of a small British warship which was anchored 100 miles (160 kilometers) up the Yangtze River in China during a very hot spell in the summer of 1934. Twelve out of 18 men who went swimming subsequently exhibited characteristic clinical symptoms of schistosomiasis japonica, and 2 of the 12 presented signs of severe involvement of the central nervous system. The period of exposure was from July 4 to 9, 1934, and the first patient reported sick on August 15, an incubation period of six weeks. On the next day, this patient suddenly became semicomatose and exhibited flaccid paralysis of both upper extremities. In addition to a temperature of 103 F. and rales in the bases of both lungs, he had intense hyperreflexia with a bilateral Babinski sign, extreme drowsiness and incontinence. He was comatose for ten days, with retrograde amnesia for the entire period. A differential white blood cell count showed 52 per cent eosinophils. During the period of coma, the spinal fluid was found to be normal except that the colloidal gold curve was "syphilitic" in type, despite repeatedly negative Kahn reactions of the fluid. Slow, but complete,

10. Africa, C. M., and Sta. Cruz, J. Z.: Eggs of Schistosoma Japonicum in the Human Heart, in Volumen Jubilare por Prof. Sadão Yoshida, Osaka, Japan, 1939, vol. 2, pp. 113-117; cited by Vitug, Cruz and Bautista.[18]

11. Day, H. B., and Kenawy, M. R.: A Case of Bilharzial Myelitis, Tr. Roy. Soc. Trop. Med. & Hyg. **30**:223-224, 1936.

12. Egan, C. H.: An Outbreak of Schistosomiasis Japonica, J. Roy. Nav. M. Serv. **22**:6-18, 1936.

recovery occurred after the patient had been given a full course of antimony sodium tartrate.

The second patient, with the severest infection of the series, was desperately ill for two months, having reported sick on August 17, with a temperature of 103 F., intense headache, occasional chills, vague abdominal pain and slight diarrhea. The patient was drowsy and listless from the start, with increased tendon reflexes and a bilateral Babinski sign, and after a week lapsed into coma for four or five days. He then showed signs of "intense meningeal reaction," with extreme restlessness, bordering on delirium, for about five weeks. It was then noted that he had left spastic hemiplegia. The spinal fluid, obtained by both lumbar and cisternal puncture, was not remarkable. After a full course of stibophen N. F. ("fuadin"; sodium antimony III biscatechol-2,4-disulfonate), amount unknown, he gradually improved, although the paralysis never cleared completely and he was subject to sudden outbursts of unprovoked laughter. Egan attributed the symptoms in this case to a cerebral embolism involving the right middle cerebral artery, due to plugging with schistosome ova. (Commonly accepted figures on the dimensions of the ovum of S. japonicum are as follows: length, 70 to 100 microns, with an average of 89 microns; breadth, 50 to 70 microns, with an average of 66 microns.)

The outbreak reported by Egan was also described by Spiridon.[13]

In 1936 Edgar [14] reported a case of epilepsy in a British naval officer who earlier had served in China for four years; operation revealed that the seizures were due to the deposition of ova of S. japonicum in the brain. Although there was no typical aura, the patient noticed "closing in" in the field of vision on his right just prior to each attack, of which he had three in all prior to surgical intervention. Neurologic examination revealed that the response of the right knee jerk was stronger than that of the left and that the muscles of the right side of the face seemed weaker than those of the left side. No sensory changes were noted, but a paracentral scotoma was found in the inferior temporal quadrant on the right. The preoperative diagnosis was glioma. At operation, a yellowish tumor, "sharply demarcated from the rest of the brain," was observed in the left temporoparietal region and was removed without difficulty. The operation was followed by slight right hemiparesis, involving the arm more than the leg, and an increase in the speech defect. The latter was still present one month after operation, but the hemiparesis had completely disappeared. The tumor was spherical and approximately 1 inch (2.5 cm.) in diameter, and frozen sections

13. Spiridon, J. T.: Schistosomiasis Japonica: An Account of an Outbreak, J. Trop. Med. **39**:161-164, 1936.

14. Edgar, E. H.: Report on a Case of Epilepsy Due to Infection by Schistosoma Japonicum, J. Roy. Nav. M. Serv. **22**:150-153, 1936.

revealed the ova of S. japonicum. The ova were also observed in the stools in this case, and there was a high degree of eosinophilia in the peripheral blood smear.

Greenfield and Pritchard,[15] in 1937, described 2 cases of cerebral involvement with the ova of S. japonicum, 1 of which has been referred to previously in Edgar's article.[14] The second case was that of a naval officer, aged 25, who fell on his head while playing cricket on July 4, 1930. Three days later he began to have headaches in the left parietal area, followed by vomiting. One month later right lower quadrantic hemianopsia was present, together with right hemiparesis. Two neurosurgical operations were performed; the first, performed on August 11, consisted in an exploratory craniotomy in the region of the left occipital lobe and revealed no abnormality. The defect in the visual fields subsequently enlarged to include a considerable portion of the upper halves of both fields, and there were intense papilledema, hemorrhage and exudate in both optic fundi. There were mild paralysis of the right side of the face, pronounced weakness of the right arm and ataxia of both limbs on the right side with increased tendon reflexes. On September 15, a second operation was performed and a large tumor removed from the upper left parieto-occipital region of the brain. Nine months later the patient still had right homonymous hemianopsia and some loss of position sense, form sense and two point discrimination in the right hand. Otherwise, the neurologic findings were within normal limits. The stools were positive for ova of S. japonicum in this case. Histologic examination of the material removed at operation revealed that the minute abscesses seen grossly consisted of clusters of ova, often surrounded by radially arranged fibroblasts and endothelial cells, with a few round cells among them. Multinucleated giant cells were also present. Surrounding nerve cells revealed advanced degenerative changes. The blood vessels (veins), even at a distance from a focus, were infiltrated with plasma cells. The authors expressed the belief that the adult parasites somehow arrive in the lateral sinus and pass up the posterior anastomotic vein, to lay eggs in small venous radicles entering this vessel.

Bayoumi[16] described (1939) another case of involvement of the spinal cord due to S. haematobium in a farmer aged 20, who died one month after admission to the hospital. Calcified ova were observed in the substance of the spinal cord and in the nerve roots, both singly and in nests. They were surrounded by dense gliosis, without much cellular reaction. Ova were also seen in the genitourinary tract, but the brain was not examined.

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15. Greenfield, J. G., and Pritchard, E. A. B.: Cerebral Infection with Schistosoma Japonicum, Brain **60**:361-363, 1937.

16. Bayoumi, M. L.: Bilharzial Myelitis, J. Egyptian M. A. **22**:457-461, 1939.

Hoff and Shaby,[17] in 1939, presented 4 cases of infection of the central nervous system with S. haematobium. In all cases the infection responded well either to stibophen or to antimony potassium tartrate U. S. P.; hence the diagnoses were clinical only and were not confirmed histologically.

In 1941 Vitug and associates[18] described 2 cases of schistosomiasis of the brain in Filipino natives. In the first case repeated jacksonian seizures occurred, and there developed a cruciate hemiplegia (with involvement of the upper right and lower left extremities), a Kernig sign and dysarthria. Three lumbar punctures revealed nothing diagnostic. The authors described in detail the gross and microscopic lesions, of which the plugging of many of the capillaries of the choroid plexus with ova of S. japonicum was an interesting feature. The second case was that of a man aged 49 from Samar, who was admitted with right hemianesthesia and hemiparesis and who exhibited spasm of the right side of the face and athetoid movements of the fingers of the right hand. Three spinal punctures revealed a cell count of 1 to 10 cells per cubic millimeter, with some increase in pressure on the first test, but the fluid was otherwise normal. Eggs of S. japonicum were observed in the stools (as well as the ova of the hookworm, Ascaris and Trichuris). The authors expressed their opinion that the favorable response to stibophen made the diagnosis plausible.

Espin,[19] in 1941, reported a case of schistosome myelitis, the first to be recognized in Venezuela, in a man aged 30; the course of the illness was rapidly downhill, ending in death fifty days after onset. Ova of S. mansoni were observed in abundance in sections of the thoracolumbar segment. The Wassermann reaction of the spinal fluid, however, was reported as 4 plus, while that of the blood was 2 plus. On further study of the sections, the author[20] reported the presence of small inclusion bodies within the motor nerve cells of the affected medullary zone, which he called pseudo-Negri bodies. So far as is known, such bodies had not previously been reported, nor has Espin's observation been confirmed.

In summary, then, a review of the available literature on this subject up to the onset of World War II discloses the following distribution of cases in which manifestations referable to the central nervous

17. Hoff, H., and Shaby, J. A.: Nervous and Mental Manifestations of Bilharzia and Their Treatment, Tr. Roy. Soc. Trop. Med. & Hyg. **33**:107-111, 1939.

18. Vitug, W.; Cruz, J. R., and Bautista, L. D.: Schistosomiasis Involving the Brain: Report of Two Cases, J. Philippine M. A. **21**:291-299, 1941.

19. Espin, J.: Mielitis producida por huevos de Schistosoma mansoni, Rev. Policlín. Caracas **10**:245-249, 1941.

20. Espin, J.: Hallazgo de corpusculos semejantes a los de negri en un cas de mielitis bilharziana, Rev. Policlín. Caracas **10**:327-336, 1941.

system were plausibly explained by infection with various schistosomes: S. mansoni, 3 cases; S. haematobium, 7 cases, and S. japonicum, 14 cases (total, 21 cases). As has been seen, the tendency of S. mansoni and S. haematobium to localize in the spinal cord and of S. japonicum to localize in the brain is striking and accounts for the varying neurologic syndromes seen with each organism. The clinical symptoms resulting from invasion of the spinal cord by the first two parasites are mainly those of myelitis or compression of the cord, while localization of the ova of S. japonicum in various areas of the brain has been responsible for a wide variety of diffuse and localizing neurologic signs. In 37 per cent of all cases, demonstration of schistosome ova within the central nervous system established the diagnosis etiologically. The data in these cases, as well as in the cases which have occurred in World War II, are summarized in table 1

TABLE 1.—*Summary of Data on Cases of Schistosomiasis with Symptoms Referable to the Central Nervous System Occurring from 1889 to May 1946*

Organism	Total No. of Cases	Clinical Diagnosis Only	Mortality	Spinal Cord		Brain	
				Examined	Eggs Found	Examined	Eggs Found
A. All Recorded Cases Occurring from 1889 to May 1946							
S. mansoni	3	None	3 (100%)	3	3	0	—
S. haematobium	7	4 (68%)	3 (43%)	3	3	1	0
S. japonicum	41	28 (68%)	5 (12%)	4	None	13	13
Total	51	32 (63%)	11 (21%)	10	6 (60%)	14	13 (93%)
B. Schistosomiasis Japonica: Comparison of Periods 1 and 2							
Period 1 (1889-Oct. 1944)	14	6 (43%)	4 (29%)	3	None	8	8
Period 2 (Oct. 1944 to May 1946)	27	22 (81%)	1 (4%)	1	None	5	5
Total	41	28 (68%)	5 (12%)	4	None	13	13 (100%)

PERIOD 2 (October 1944 to May 1946).—Twenty-seven additional cases have been observed during World War II, 21 of which have previously been published.

With the landing of American troops on Leyte, in the Philippines, on Oct. 20, 1944, military operations necessitated unavoidable exposure to infection with S. japonicum, and within the past year the clinical literature on schistosomiasis japonica has increased considerably.

In a discussion of the early symptoms of the disease, as seen in United States Army personnel on Leyte, Thomas and Gage [21] stated in August 1945 that symptoms referable to the central nervous system were prominent in 2 of a series of 41 cases and in 1 other case not included in their series. In the last case the patient was admitted in coma; he showed some response to treatment but relapsed and died. According to their description, the "brain and cord appeared grossly normal."

21. Thomas, H. M., Jr., and Gage, D. P.: Symptomatology of Early Schistosomiasis Japonica, Bull. U. S. Army M. Dept. **4**:197-202, 1945.

Detailed neurologic examinations were not reported, but in these 3 cases there were weakness of the arms and spasticity of the legs, with increased tendon jerks. In 2 cases ankle clonus was present bilaterally. In 1 (case 5) [22] the patient was disoriented on admission; the end arteries of his feet became occluded, but he improved greatly after treatment with stibophen. Sensation was normal in each case.

In a brief reference, Tillman,[23] in November 1945, reported 7 cases (5, 6, 7, 8, 9, 10 and 11), also among United States Army personnel, of schistosomiasis japonica contracted during the Leyte campaign in which there occurred various manifestations referable to the central nervous system, among them weakness of the arms or legs, hyperreflexia, aphasia and disturbed sensorium. The patients recovered but were followed only three months, at which time "some residual changes were present."

Carroll [24] described 5 additional cases of the cerebral infection in American soldiers (cases 12, 13, 14, 15 and 26). The fifth case was that of a combat engineer aged 26 who was heavily exposed to infected fresh water during November 1944 while building bridges on Leyte. Clinical onset occurred on Jan. 14, 1945 (six to eight weeks later) with abdominal cramps and stiffness of the neck. He was hospitalized on January 29, and eosinophilia, with 50 per cent eosinophils, was observed. He received 40 cc. of stibophen on clinical grounds alone. On February 23 (eleven to thirteen weeks after the first potential exposure), immature ova of S. japonicum were observed on examination of the stool. On May 17 he had a clonic convulsion of the left side while lying in bed. This was repeated five hours later. On May 20 he had another left-sided (jacksonian) seizure, with recurrence one hour later. Four days later weakness of the entire left side was noted; this progressed to complete left hemiplegia. Craniotomy on the right side, performed overseas on June 15, revealed no significant pathologic condition, and the patient was evacuated to the United States for further observation and treatment. Roentgenograms of the skull, ventriculograms and studies of the visual fields were reported to show nothing significant. Follow-up studies in this case were incomplete. Since only immature eggs were observed in the stools, the diagnosis in this case is less certain than in the other 4 cases reported.

Watson and associates [25] described in detail clinical and laboratory observations in the case of an American infantryman aged 20 (case 17), who landed on Leyte about Dec. 1, 1944 and was first exposed to

22. All case numbers in the text correspond to case numbers in the appendix.

23. Tillman, A. J. B.: Cerebral Manifestations of Schistosomiasis Japonica, Bull. U. S. Army M. Dept. **4**:492, 1945.

24. Carroll, D. G.: Cerebral Involvement in Schistosomiasis Japonica, Bull. Johns Hopkins Hosp. **78**:219-234, 1946.

25. Watson, C. W.; Murphey, F., and Little, S. C.: Schistosomiasis of the Brain Due to Schistosoma Japonicum, to be published.

infected fresh water on December 12. There developed intermittent cough, pain in the right upper abdominal quadrant, fever, diarrhea and severe vomiting, together with persistent leukocytosis and a high degree of eosinophilia. When stools examined overseas, on April 2 and 6, 1945, were found to contain ova of S. japonicum, he was given a course of emetine hydrochloride (0.6 Gm.). One hundred and fifty-six days after his initial exposure, he had a grand mal seizure, followed by nine others prior to his admission to an Army general hospital in the United States. Involvement of the central nervous system with schistosomes was not suspected overseas. When neurologic examination pointed to a focus of irritation in the left cerebral hemisphere (confirmed electroencephalographically and by roentgenograms of the skull), two neurosurgical procedures were carried out, and the underlying pathologic process, which grossly seemed similar to an infiltrating glioma, proved to be due to disseminated pseudotubercles containing ova of S. japonicum (observations confirmed by the United States Army Medical Museum) In addition to neurosurgical treatment, the patient also received 75 cc. of stibophen intramuscularly, together with large amounts of diphenylhydantoin sodium and phenobarbital, with considerable improvement both in his general condition and with respect to reduction in the number and severity of his seizures. He is now under observation in this hospital, after transfer from a neurosurgical center.

Maltby and Schmidt [26] presented the case of an American soldier, aged 24 (case 18), who had onset of a productive cough while on Leyte but manifested no other clinical or cerebral signs of schistosomiasis japonica until "a few months" later (May 1945), at which time he was stationed on Okinawa. After a transient psychotic episode, he began to have headaches and in October 1945 noted parethesias involving the right hand. On November 4 and 18 he lost consciousness and had convulsive movements of the tongue, the right side of the face and the right hand, followed by motor aphasia. Several similar episodes occurred prior to his admission to a United States Army general hospital in this country on November 30. After preliminary studies, a craniotomy was performed in the left parietal area on December 13; an irregular, "rubbery" mass, measuring 3 by 20 by 23 mm., was partially removed from the midparietal region, and eggs of S. japonicum were demonstrated in the microscopic sections. After operation, eggs of S. japonicum were observed in the stools, and the patient was given a course of 75 cc. of stibophen intramuscularly. "Remarkable" recovery followed, and the ova temporarily disappeared from the stools. At the time of his transfer to this hospital for further specific treatment (two months after operation) the only abnormal neurologic findings were slight residual weakness of the muscles of the right side of the face

26. Maltby, G. L., and Schmidt, J. R.: Schistosomiasis of the Cerebrum Simulating Brain Tumor, to be published.

and barely perceptible slurring of speech. Another patient (case 19) who was operated on by the authors has recently come under our care.

Four additional cases (20, 21, 22 and 23) have been studied in the United States Army personnel at Mayo General Hospital, Galesburg, Ill., by Johnson, Spiegel, Uihlein and Perkins, and will be reported elsewhere.[27] In 2 of these cases (20 and 21) craniotomies were performed and the eggs of S. japonicum demonstrated in the brain. Although signs and symptoms of an expanding intracranial process have appeared in the other 2 cases, surgical intervention has been delayed pending the results of specific treatment with antimony potassium tartrate and further observation, with more exact localization of the lesions.

Since the invasion of Leyte on Oct. 20, 1944, then, six separate groups of investigators have recorded 21 new cases in which complications of the central nervous system accompanied infection with S. japonicum.

Of these 21 cases, 12 have subsequently been followed at this hospital. Six additional cases (cases 1 to 4, 16 and 24) have not previously been reported. Five of these have been followed in this hospital, and cases 2 and 16 are presented in the appendix in condensed form. Case 24, which was not followed here, has not been reported. In other words, of 27 cases added to the literature on schistosomiasis involving the central nervous system occurring since October 1944 (as tabulated in the "Appendix"), we have had an opportunity to study 17 at the Moore General Hospital.

These cases represent approximately 2.0 per cent of the total series of 800 cases of Asiatic schistosomiasis observed at this hospital (a tropical disease center). The 27 known cases of schistosomiasis involving the central nervous system which have occurred among American military personnel since October 1944 constitute approximately 2.3 per cent of all known cases (1,200) of schistosomiasis japonica contracted during the Leyte campaign. Furthermore, this increases from 14 to 41 the total number of reported cases of complications of the central nervous system associated with infection with S. japonicum. With 3 exceptions, the series to be reported are those of United States Army personnel who contracted the disease on Leyte.

Each patient seen at this hospital was followed a minimum of three months from the date of admission, and some have been under observation as long as twelve months. Presentation of selected case histories with enumeration of the residual signs at discharge should offer considerable prognostic assistance in similar cases and may stimulate earlier recognition of what we believe to be a fairly characteristic neurologic syndrome.

27. (*a*) Speigel, I. J.: Cerebral Schistosomiasis, J. Neurosurg. **4**:72-80, 1947. (*b*) Uihlein, A., and Perkins, R. F.: Cerebral Schistosomiasis Japonica, to be published.

In 5 out of 8 cases in this series in which operation was performed, ova of S. japonicum were observed in sections taken from the central nervous system. In the other 3 surgical cases no tissue was removed for microscopic examination. In a fatal case reported by Thomas and Gage [21] the brain and spinal cord were described as normal. In all other cases in this series the diagnosis of schistosomiasis of the central

TABLE 2.—*Data on Source of Infection and Time of Onset in All Known Cases of Schistosomiasis Japonica with Complications Referable to the Central Nervous System Reported in United States Army Personnel Since Oct. 20, 1944**

Case No.	Age, Yr.	Race	Source of Infection	Interval from First Potential Exposure to Clinical Onset	Interval from Clinical Onset
Group 1: Nonoperative Cases					
1 †‡	24	W	Leyte, P. I.	22 wk.	3 days
2 †‡	27	W	Leyte, P. I.	6 wk.	2 wk.
3 †‡	24	W	Leyte, P. I.	6 wk.	(Coincident)
4 †‡	26	W	Leyte, P. I.	(?) 10 wk.	7 wk.
5 †	26	W	Leyte, P. I.	6 wk.	3 wk.
6	25	W	Leyte, P. I.	4 wk.	2 wk.
7 †	21	W	Leyte, P. I.	12 wk.	3 wk.
8 †	28	W	Leyte, P. I.	8 wk.	3 wk.
9 †	27	American Indian	Leyte, P. I.	6 wk.	7 wk.
10 †	24	W	Leyte, P. I.	10 wk.	(Coincident)
11	29	W	Leyte, P. I.	7 wk.	2 wk.
12 †	21	W	Leyte, P. I.	6 wk.	2 wk.
13 †	30	W	Leyte, P. I.	7 wk.	5 wk.
14 †	20	W	Leyte, P. I.	19 wk.	5 wk.
15 †	21	W	Leyte, P. I.	17 wk.	6 wk.
Group 2: Operative Cases or Cases in Which Symptoms Simulated Brain Tumor					
16 †‡	26	W	Mindanao, P. I.	(?) 8 wk.	6 mo.
17 †	29	W	Leyte, P. I.	3 wk.	4½ mo.
18 †	24	W	Leyte, P. I.	(?) 3 mo.	(Coincident)
19 †‡	27	W	Leyte, P. I.	(Asymptomatic)	1 yr. after 1st exposure
20	23	W	Leyte, P. I.	2½ mo.	2½ mo.
21	28	W	Leyte, P. I.	1 mo.	1 mo.
22	20	W	New Guinea (?)	?	2 yr. after 1st exposure
23	40	W	Mindanao, P. I.	?	9-12 mo. after 1st exposure
24 ‡	29	W	Leyte, P. I.	(Asymptomatic)	3 mo. after 1st exposure
25	26	W	Leyte, P. I.	9 wk.	4 mo.

* This table does not include 2 of the cases (26 and 27) reported briefly by Thomas and Gage [21]; it does include their third case, which corresponds with case 5 in this series and which has been reported elsewhere in detail by Johnson and Berry.[34k]

† The case in question was observed and followed at Moore General Hospital.

‡ The double dagger indicates cases not previously reported.

nervous system was based on highly suggestive clinical and laboratory evidence.

As far as could be determined, the family history in each case was noncontributory. There was no significant past history of neurologic or mental disorders in any case. Significant items in the past medical history will be noted when pertinent.

For purposes of clarity, the cases in this series are listed in table 2 and are grouped according to their salient neurologic features; i. e., group 1 (cases 1 to 15) includes all nonsurgical cases with diffuse

and/or focal neurologic signs, while group 2 (cases 16 to 25) includes all cases with symptoms of an expanding intracranial lesion simulating tumor of the brain.

ANALYSIS AND COMMENT

In the course of many exanthems, development of complications referable to the nervous system is not rare.[28] While the complication may take the form of diffuse meningoencephalitis, transitory monoplegia or hemiplegia, with or without aphasia, may also be seen. The underlying pathologic change in hemiplegia is usually attributed to "cerebral embolism."

As Wechsler[29] pointed out, however, closer scrutiny reveals that the cause is much oftener thrombosis, since particles large enough to occlude a cerebral blood vessel of any appreciable size cannot possibly break through the barrier of the pulmonary capillaries. An exception occurs in cases of patent foramen ovale, i. e., so-called paradoxic embolism.

In addition to the long list of diseases of bacterial, viral or rickettsial origin which may have sequelae referable to the central nervous system, there are a number of parasitic infections besides schistosomiasis in which cerebral involvement is well recognized.[30] Among the commonest of these are trichinosis, cysticercosis (due to the larval stage of the pork tapeworm, Taenia solium), "hydatid disease" (echinococcosis, due to Echinococcus granulosus) and paragonimiasis (due to P. westermani, an Oriental lung fluke). Although the central nervous system is limited in the ways in which it is able to respond to various toxic or disease-producing agents, the pathologic lesion resulting from cerebral invasion by each of these parasites is fairly distinctive.

THEORIES OF ROUTE OF INVASION BY OVA OF S. JAPONICUM

Each author interested in this problem has ventured a different opinion on the mechanism by which the ova of this trematode somehow find their way into the cerebral circulation.

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28. Wilson, S A. K.: Neurology, London, Edward Arnold & Company, 1944, vol 1, pp. 55-80.

29. Wechsler, I. S.: A Textbook of Clinical Neurology, ed. 5, Philadelphia, W. B. Saunders Company, 1943, p. 345.

30. (*a*) Chalgren, W. S., and Baker, A. B.: Tropical Diseases: Involvement of the Nervous System, Arch. Path. **41**:66-117 (Jan.) 1946. (*b*) Austregesilo, A.: Nervous Disorders in Certain Tropical Diseases, Rev. neurol., **1**:1-21, 1927; abstracted, Arch. Neurol. & Psychiat. **18**:596-599 (Oct.) 1927. (*c*) von Henneberg, R.: Die tierischen Parasiten des Zentralnervensystem, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 14, pp. 286-352.

Basically, there seem to be two divergent schools of thought: (*a*) investigators who advance the theory of direct deposition, e. g., Shimidzu[8] and Greenfield and Pritchard[15]; and (*b*) supporters of the theory of indirect (or embolic) deposition, which is upheld by most other investigators.[31] The proponents of the theory of embolization have invoked a variety of ingenious mechanisms, such as cardiac septal defect and anastomotic channels—for example, the inferior hemorrhoidal or vertebral venous plexuses[32]—to explain how the ova manage to by-pass the liver-lung barrier.

It is entirely possible that both mechanisms may be operative. In defense of the first postulation, there is experimental evidence that the adult worms may occasionally arrive in the cerebral circulation. This is contained in a brief statement in Shimidzu's[8] article, in which he affirmed that a second Japanese investigator, Fujinami, noted paired adult schistosomes in the cerebral veins of monkeys exposed to a heavy concentration of cercariae. As far as we know, a similar observation in human operative or postmortem material has never been reported. This does not preclude the possibility that the adult parasites may be present in cerebral blood vessels at some distance from the main pathologic process incited by the ova. Furthermore, the liver-lung barrier might be avoided by the presence of the adult worms in the pulmonary vessels, as has been reported for S. mansoni.[33] In summary, then, while it is likely that single ova may reach the cerebral circulation by various channels, it is difficult to explain the occurrence of "nests" of eggs within the brain on any basis other than close proximity of the adult female worm, i. e., perhaps in the lateral sinus, as suggested by Greenfield and associates.[15] While of considerable theoretic interest, these questions still remain unsolved.

PATHOLOGIC ANATOMIC CHANGES

Once the ova of S. japonicum have invaded the central nervous system, by whatever route, they are capable of producing an intense reaction both in the cerebral blood vessels, where they may lodge, and in the surrounding parenchyma of the brain.

Apparently, the pathologic reaction resulting from the ova may be due to one or more factors: (*a*) their physical presence, causing occlusion of cerebral vessels and passive congestive changes; (*b*) foreign protein, and (*c*) possibly, a chemical toxin elaborated within the ovum. Faust and Meleney[1] expressed the belief that this pyogenic toxin is

31. Yamagiwa.[2] Tsunoda and Shimamura.[3] Houghton.[4] Nieva.[9] Africa and Sta. Cruz.[10] Egan.[12] Vitug and others.[18]

32. Batson, O. V.: The Role of the Vertebral Veins in Metastatic Processes, Ann. Int. Med. **16**:38, 1942.

33. Craig, C. F., and Faust, E. C.: Clinical Parasitology, ed. 3, Philadelphia, Lea & Febiger, 1943, p. 365.

secreted as long as the miracidium is alive and escapes through the porous shell of the ovum wherever it lodges. While most of the ova seen in sections of the brain have been immature, some have been seen with miracidia [8] within the egg shells.

Many of the gross and microscopic lesions resulting from localization of these ova in the central nervous system have already been described in the review of the literature,[34] but a few prominent features bear reemphasis at this point.

Eggs of S. japonicum have been demonstrated in practically all areas of the brain, but seem to have been observed in greater abundance in the pia-arachnoid, cortex, subcortex, basal ganglia, internal capsules and choroid plexuses of the lateral ventricles. Calcification and formation of scar tissue were prominent features of the healing process.

Possibly the best description of the microscopic changes in such cases is that by Shimidzu,[8] who recognized four more or less concentric zones of reaction around the imprisoned ova: (*a*) a central zone of necrosis with a few spindle-shaped cells and eosinophils; (*b*) a middle zone of epithelioid cells with some lymphocytes; (*c*) a cellular layer composed of lymphocytes, plasma cells, eosinophils, fibroblasts and an abundant lattice work of *Gitterzellen*, and, finally, (*d*) a peripheral zone, demonstrable only with special glial stains, containing protoplasmic astrocytes, "Hortega glial cells" and abundant lipid cells. Within the middle and cellular zones he noted a tendency to radial arrangement of the epithelioid cells and fibroblasts. Multinucleate foreign body giant cells have also been reported [35] in some cases but may be absent in others.[25] The surrounding ganglion cells showed advanced degenerative changes. While intense infiltration of neighboring cerebral veins is common, no investigator observed any evidence of pathologic change in the cerebral arteries or of the immediate presence of the adult worms.

This description agrees closely with the account by Faust and Meleney [1] of the basic pathologic lesion of the disease, which they called "the schistosomiasis abscess." In many ways, this granulomatous reaction resembles the tuberculous lesion, hence the synonym "pseudotubercle" for the hard, white, pinpoint-to-pinhead-sized lesions to be seen scattered over the surface of the cortex in these cases.

Representative sections of brain tissue (furnished by the Army Medical Museum, Washington, D. C.) are illustrated with accompanying photomicrographs.

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34. (*a*) Yamagiwa.[2] (*b*) Tsunoda and Shimamura.[3] (*c*) Houghton.[4] (*d*) Shimidzu.[8] (*e*) Edgar.[14] (*f*) Greenfield and Pritchard.[15] (*g*) Vitug and others.[18] (*h*) Watson and others.[25] (*i*) Maltby and Schmidt.[26] (*j*) Footnote 27. (*k*) Johnson, A. S., Jr., and Berry, M. G.: Asiatic Schistosomiasis: Clinical Features, Sigmoidoscopic Picture, and Treatment of Early Infections, War Med. **8**:156-162 (Sept.) 1945.

35. Greenfield and Pritchard.[15] Maltby and Schmidt.[26]

CLINICAL AND NEUROLOGIC FEATURES

A comprehensive analysis of the main subjective and objective findings in 25 cases, as well as a summary of pertinent laboratory data follow. The data on 2 cases (26 and 27), which are incompletely documented, are omitted.

Onset.—The rather sudden onset of major complications referable to the central nervous system was a striking feature in this series, occurring in virtually all cases (95 per cent).

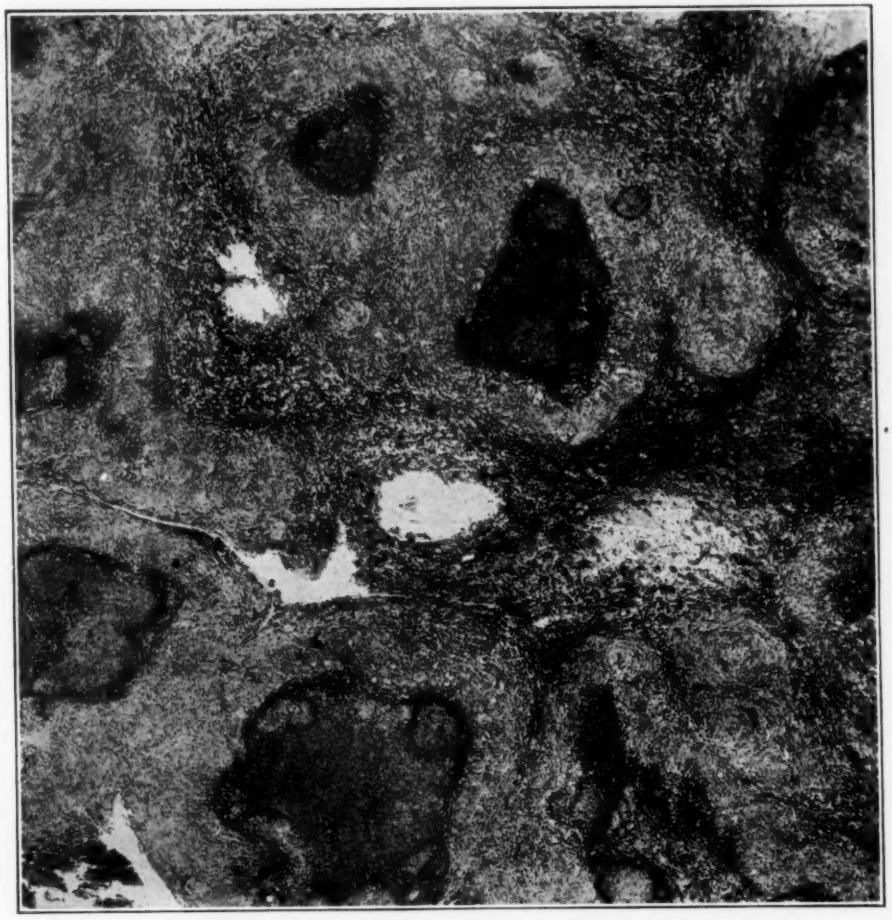

Fig. 1.—In this figure, and in the accompanying figures, the photomicrographs show lesions of the brain in cases of schistosomiasis japonica (prints furnished by the United States Army Medical Museum).

Section through the cortex in case 20 (× 25), showing numerous miliary abscesses and intense focal reaction. (United States Army Medical Museum negative no. 93469.)

The average interval from the first potential exposure to clinical onset in the cases of group 1 was ten weeks, with a range of four to

twenty-two weeks, and that for group 2 was nine weeks, with a range of three to twelve weeks. The average interval from the first recognized clinical symptoms to onset of symptoms referable to the central nervous system was 3.2 weeks (range, zero to seven weeks) for group 1 and twelve weeks (range, four to twenty-four weeks) for group 2. The average interval from the first potential exposure to onset of symptoms of involvement of the central nervous system was 12.8 weeks (range, six to twenty-four weeks) for group 1 and 22.8 weeks (range, eight to fifty-two weeks) for group 2. In 2 cases (cases 19 and 24, or 8 per cent) abnormalities referable to the central nervous system proved to be the only presenting feature of the disease.

The distribution of the cases on the basis of the interval from the first potential exposure to onset of symptoms referable to the central nervous system is shown in the following tabulation.

Interval, Wk.	Group 1 (15 Cases)	Group 2 (10 Cases)
0- 5	None	None
6-10	7 (46%)	1 (10%)
11-15	4 (27%)	2 (20%)
16-20	1 (7%)	2 (20%)
21-25	3 (20%)	1 (10%)
25	None	4 (40%)

Prodromal Symptoms.—As indicated in the tabulation, the five most important clinical clues to the diagnosis of early schistosomiasis japonica [36] occurred in the following distribution in this series:

	Group 1 (15 Cases)		Group 2 (10 Cases)		Total
	No. of Cases	Per-centage	No. of Cases	Per-centage	Per-centage
History of exposure	15	100	10	100	100
Fever	15	100	6	60	84
Gastrointestinal complaints	14	93	5	50	76
Cough	9	60	2	20	44
Urticaria or angioneurotic edema	9	60	1	10	40

These tabulations serve to emphasize the increased difficulty in diagnosis in group 2 (i. e., cases of symptoms of an expanding intracranial lesion simulating brain tumor) because of (*a*) the longer interval between exposure and onset of symptoms referable to the central nervous system, during which the patient will usually have been evacuated from the original site of infection, and (*b*) the higher incidence of an atypical early phase of the disease, without fever, allergic phenomena or gastrointestinal or pulmonary symptoms.

Exposure.—It was not possible in this series to relate either the duration (range, from a few days to six months) or the number of

36. (*a*) Billings, F. T.; Winkenwerder, W. L., and Hunninen, A. V.: Studies on Acute Schistosomiasis Japonica in the Philippine Islands, Bull. Johns Hopkins Hosp. **78**:21-56, 1946. (b) Thomas and Gage.[21]

exposures (one to multiple) to the subsequent development of abnormalities of the central nervous system, although, unquestionably, these are important factors in determining the severity of the usual clinical case.[37]

Symptoms.—Since a large percentage of patients (84 per cent) were febrile at one time or other (usually during the first three months of the clinical illness), it is difficult to evaluate the minor degrees of

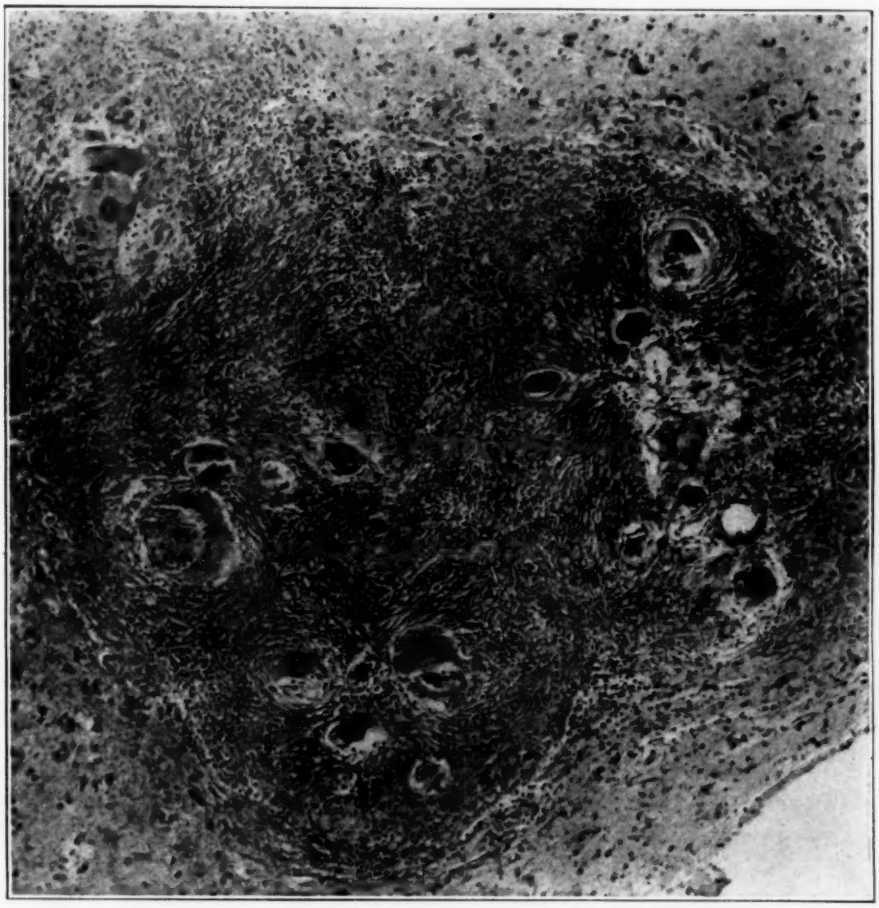

Fig. 2 (case 17).—Slightly higher magnification (× 100) of an area of the cortex photographed in figure 1, showing intense inflammatory reaction, with scattered eggs and giant cells. (United States Army Medical Museum negative no. 93473.)

headache and associated symptoms which were reported. This is especially evident when one attempts to relate these subjective dis-

37. (*a*) Most, H.; Kane, C. A.; Katzin, B.; Lavietes, P. H., and Schroeder, E. F.: Schistosomiasis Japonica in the First Year of Infection, unpublished data. (b) Billings and others.[36a]

turbances to major complications of the central nervous system. A few should be noted, however, at this point.

Headache: This was present in all cases. In most of the nonsurgical cases, i. e., in group 1, this complaint was not of localizing value and was either transitory or intermittent. In 4 to 10 cases in the operative group (cases 17, 18, 19 and 20), headache was of definite localizing value, occurring on the same side as the major intracranial

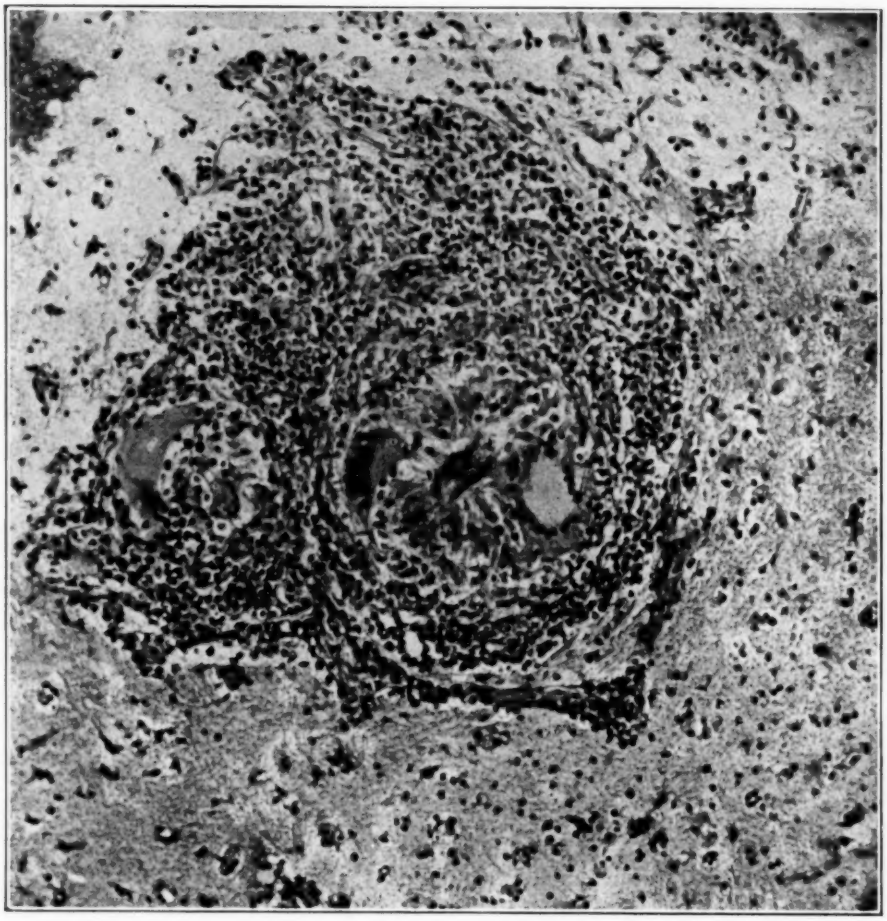

Fig. 3 (case 18).—Miliary abscess (× 150), showing a focal granulomatous lesion with wrinkled remains of an egg (in center), adjacent giant cell and intense zone of reaction. (United States Army Medical Museum negative no. 93480.)

process. In all cases in this group headache was a severe, persistent symptom, relieved only by spinal tap or operative intervention.

Disturbances of the Sensorium: The incidence of these disturbances was 100 per cent. They varied from momentary periods of confusion resembling attacks of petit mal to prolonged periods of unconsciousness, lasting hours in cases in which convulsive seizures occurred.

In the nonsurgical cases disorientation and confusion at onset constituted a striking feature, lasting as long as two weeks in some instances. In most of these cases there were listlessness and apathy, but in 4 out of 15 cases (2, 9, 11 and 12) extreme restlessness, at times bordering on mania, was present. None of the patients in group 1 were truly comatose at any time; however 6 patients (2, 3, 4, 8, 9 and 10) were semicomatose for periods ranging from two days up to one week (case 4). No convulsions occurred in this group.

In all the operative cases the patients had convulsions of one type or other, and were comatose for periods up to twelve hours (case 16). All types of seizures were noted: sensory, motor (jacksonian, tonic-clonic, adversive and atypical) and psychomotor, and these were associated with a variety of sequelae, including motor aphasia, defects of the cranial nerves and visual fields, alexia, micropsia (case 17) and postictal confusion, together with defects of the pyramidal tracts, usually consisting in hemiparesis (case 16) or hemiplegia (case 25).

Ruesch [38] recently reviewed disturbances of consciousness due to a variety of intracranial processes and suggested that they all have a "common physiological background," i. e., anoxia. In addition, he accumulated statistical evidence which seems to indicate that prolonged drowsiness and confusion are most often found in cases of pathologic intracranial processes with diffuse lesions which have a predilection for localization in the basal ganglia and the left temporoparietal lobe.

Visual Upsets: Blurred vision (group 1) was present in 27 per cent (cases 1, 2, 3 and 5), and defects of the visual fields (group 2) were noted in 80 per cent (cases 16 to 22 and 24).

A variety of visual disturbances have been reported in these cases, ranging from simple angioneurotic swelling of the eyelids to intense papilledema, a bizarre retinal lesion (case 2) and various defects of the visual fields (operative cases). As far as is known, all reported visual aberrations have proved to be transitory, with 1 exception (case 24).

Several seizures in case 17 began with visions of the surroundings on a lilliputian scale (micropsia), which are usually attributed [39] to a lesion of either temporal lobe. Visual agnosia was absent, but one of these attacks was followed by a right homonymous field defect with sparing of the macula. Sometimes a prodrome of alexia preceded the attacks.

Speech Disturbances: These were present in 48 per cent of cases. Minor speech disturbances (dysarthria of one type or other) were present in 6 cases in group 1 (1, 5, 7, 8, 9 and 10) and were usually

38. Ruesch, J.: The Diagnostic Value of Disturbances of Consciousness, Dis. Nerv. System **5**:69-83, 1944.

39. Brock, S.: The Basis of Clinical Neurology, ed. 2, Baltimore, Williams & Wilkins Company, 1945, pp. 287-288.

transitory. In 2 cases in the same group (8 and 10) at least a partial true motor aphasia was apparently present. Both patients were right handed; the first patient had spastic quadriplegia, and the second flaccid left hemiparesis, as the major neurologic defect.

In 6 out of 10 cases in the operative group (cases 16 to 20, and 23) true motor aphasia was also present. In each of these cases operation revealed a space-occupying lesion in the dominant (left) cerebral hemisphere. In cases 16 and 18 the aphasia cleared up entirely after operative intervention and specific treatment for schistosomiasis. The aphasia was still present intermittently (postictal) in case 17 six months after the last craniotomy, but was greatly improved.

Weakness of One or More Extremities: This complaint was present in all cases at one time or another. Characteristically, its onset was

TABLE 3.—*Incidence of Symptoms in Twenty-Five Cases of Schistosomiasis Japonica with Involvement of the Central Nervous System*

Complaint	Group 1 (15 Cases)*		Group 2 (10 Cases)†		Over-All Incidence, %
	No. of Cases	Percentage	No. of Cases	Percentage	
Headache	15	100	10	100	100
Disturbance of sensorium	15	100	10	100	100
Weakness of extremities	15	100	10	100	100
Visual upsets	7	45	8	80	60
Incontinence	12	80	2	20	56
Sensory disturbance (paresthesia, anesthesia)	5	33	8	80	52
Speech disturbances	6	40	6	60	48
Ataxia	9	60	3	30	48
Vertigo	1	7	5	50	24
Sore or stiff neck	3	20	2	20	20
Deafness	0	..	2	20	8
Tinnitus	0	0	1	10	4
Trophic disturbance	1	7	0	..	4

* Nonoperative cases.
† Operative cases or cases in which the symptoms simulated cerebral tumor.

sudden; i. e., it appeared in terms of hours rather than of days or weeks. The duration and type, with residual findings, are outlined in the sections on neurologic signs and prognosis, to follow. The symptoms in these cases are summarized in table 3.

General Physical Examination.—Enlargement of the liver was noted in 9 cases of group 1 and in 2 cases of group 2, whereas an enlarged spleen was felt in only 1 case in each group. Because of intercurrent illness in many cases, loss of weight with accompanying malnutrition was difficult to evaluate, but some loss of weight (from 5 to 40 pounds [2.3 to 18.1 Kg.]) was noted in virtually every case. This is a well recognized complication of acute schistosomiasis japonica.[40]

Neurologic Phenomena.—Since these signs are described in detail in the individual case histories, we shall endeavor in this section to emphasize some of the more interesting neurologic features, as well

40. Thomas and Gage,[21] Footnote 37.

as to point out the striking absence of other signs which may, perhaps, have been anticipated in patients with such a diffuse intracranial process.

GROUP 1: Nonsurgical Cases. In addition to the obvious division of all cases into those with and those without an expanding intracranial process, it is readily apparent that the 15 cases in group 1, in which operation was not indicated, may be classified roughly on the basis of other lines. This is illustrated in the following summary

	No. of Cases
Monoplegia	3 (7, 14 and 15)
Hemiplegia or hemiparesis	6 (1, 3, 5, 8, 10 and 13)
Quadriplegia	6 (2, 4, 6, 9, 11 and 12)

In 3 cases (7, 14 and 15) the motor disturbance was essentially a flaccid, probably cortical, monoplegia. In the remaining cases the motor weakness was probably due to lesions in one or both internal capsules ("capsular hemiplegias"). Associated palsies of the cranial nerve were relatively infrequently found in this group (cases 1, 4, 5, 8, 10 and 11), and there were no instances of true "alternating hemiplegias." In case 6 the picture of cruciate hemiplegia was presented at one stage, suggesting the possibility of a low bulbar lesion near the pyramidal decussation. The rapid recovery with specific therapy in some of these cases may be related to the disappearance of angioneurotic edema surrounding these tracts.[39]

In all cases, resistance to passive stretch was abnormal, with spasticity in the end stages in the vast majority, although this apparently did not develop in cases 7, 9, 11, 14 and 15. It is usually stated [41] that flaccid hemiplegia is commonly associated with sensory changes and atrophy, but this rule was not borne out in the present cases.

It is difficult to estimate just how much extrapyramidal involvement was associated with the "pyramidal" hemiplegia in these cases. However, in 10 cases a positive Hoffmann sign was reported to have been present at one time. As Tower [42] has shown, this reflex is often associated with the usual "pyramidal" hemiplegia because of a combination of pyramidal and extrapyramidal defects. In addition, in 4 cases (1, 8, 9 and 10) other symptoms (choreoathetosis, dystonia and rigidity) suggestive of involvement of the basal ganglia were present. No state resembling parkinsonism has thus far developed in this series. In 4 cases (5, 8, 10 and 11) there were symptoms definitely suggestive of involvement of cerebellar pathways, i.e., ataxia, dysmetria, confusion of laterality, adiadokokinesis and a positive Romberg sign, most of which were transitory.

41. Fulton, J. F., and Viets, H. R.: Upper Motor Neuron Lesions, J. A. M. A. **104**:357-362 (Feb. 2) 1935.

42. Tower, S. S.: The Pyramidal Tract, in Bucy, P. C.: The Precentral Motor Cortex, Urbana, Ill., University of Illinois Press, 1944, chap. 6.

Involvement of the brain stem was not common, but symptoms suggestive of lesions affecting the nuclei of the third, fourth, sixth, seventh, tenth and twelfth cranial nerves were seen in 6 cases (1, 4, 5, 8, 10 and 11).

Meningeal signs (stiffness of the neck and positive Kernig and Brudzinski signs) were seen in 2 cases (8 and 10). Soreness of the neck of myalgic origin is not an uncommon feature of the usual clinical

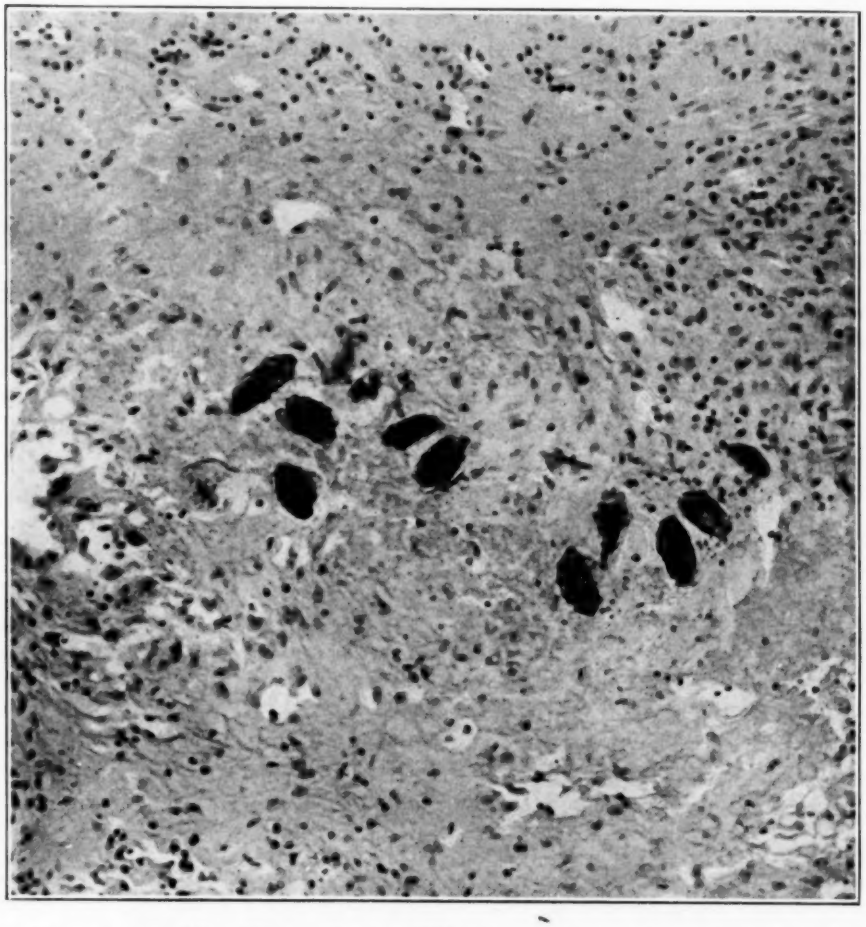

Fig. 4 (case 21).—Giant cells (× 200); note fragmented remains of an egg in association with the two upper cells. (United States Army Medical Museum negative no 93461.)

case of schistosomiasis japonica,[43] but the stiffness is severest on rotation and lateral flexion of the neck.

Diffuse encephalitis was unquestionably present in all but 1 (case 14) of 15 cases (93 per cent) in group I and probably accounts for such dis-

43. Thomas and Gage.[21] Billings and others.[36a]

orders as the prolonged and serious disturbances of the sensorium, the high incidence of incontinence and the bilateral motor involvement.

While other investigators have noted that these syndromes are mainly motor, rather than sensory, definite abnormalities in sensory discrimination, which are described in the clinical histories, have been observed in a number of cases in both groups.

The trophic disturbances that occurred in case 5 were probably due to vascular occlusion of small peripheral end arteries by ova rather than to any neurologic lesion.

Medullary, pseudobulbar or spinal involvement was not apparent in any case of this group.

Group 2: Operative Cases.—The sudden onset of complications referable to the central nervous system has already been emphasized; it should also be pointed out that in 5 cases of this group the neurologic phenomena proved to be the major presenting feature of the disease.

In the majority of cases (both in the old and in the recent literature on this subject) in which the condition has clinically simulated tumors of the brain, the lesions seem to have shown a remarkable tendency to localize in the left cerebral hemisphere.[44] A similar tendency is seen in the present series, the major pathologic process occurring in the left, or dominant, hemisphere in 7 cases.

Motor aphasia, accordingly, of varying severity and duration, was present in 6 cases (16 to 20, and 23), whereas alexia was noted in 2 cases (17 and 24).

Papilledema was present in 5 cases in which operation was performed, while various types of defects of the visual fields (chiefly homonymous hemianopsias) were found in 6 cases.

Defects of the cranial nerves in this (operative) group were more than twice as common as in group 1.

Abnormalities of sensory discrimination also were commoner than in group 1, although not so prominent as the motor and reflex disturbances resulting from involvement of the pyramidal and extrapyamidal tracts.

Hyperreflexia was noted in all cases. The Hoffmann sign was elicited in 6 cases (16, 18, 19, 21, 23 and 24), and the Babinski sign in 4 cases (19, 20, 23 and 24), of this group.

The outstanding neurologic features of all cases of the two groups are summarized in table 4.

Laboratory Studies.—Repeated smears for parasites of Plasmodium falciparum and OXK-agglutination tests gave uniformly negative results during the acute phases of the illness in the cases in which these tests were performed.

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44. Tsunoda and Shimamura.[3] Shimidzu.[8] Edgar.[14] Greenfield and Pritchard.[15] Watson and others.[25] Maltby and Schmidt.[26]

In 22 cases (88 per cent) ova of S. japonicum were not observed in the stools until after onset of symptoms referable to the central nervous system, the interval after onset ranging from two days to twelve months. In 2 cases (14 and 25), however, the diagnosis of schistosomiasis with the presence of the ova in the stools was verified prior to onset of cerebral symptoms—in 1 instance, six days, and in the other, eighty-three days. In 1 instance (case 6) ova were not demonstrated while the patient was overseas, and the patient was never rehospitalized so

TABLE 4.—*Cases of Schistosomiasis of the Central Nervous System Observed in United States Army Personnel Since October 1944, with Type of Intracranial Process Involved*

Case No.	Type of Lesion of the Central Nervous System: Focal Lesion: Pyramidal	Focal Lesion: Extrapyramidal*	Focal Lesion: Other	Diffuse Lesion: Encephalitic	Diffuse Lesion: Meningeal	Expanding Lesion
Group 1: Nonoperative Cases						
1	+	+	+	+	−	−
2	+	−	+	+	−	−
3	+	−	−	+	−	−
4	+	−	+	+	−	−
5	+	±	+	+	−	−
6	+	−	+	+	−	−
7	+	−	−	+	−	−
8	+	±	+	+	+	−
9	+	+	+	+	±	−
10	+	+	+	+	+	−
11	+	−	+	+	−	−
12	+	±	−	+	−	−
13	+	−	−	+	−	−
14	+	−	−	±	−	−
15	+	−	−	+	−	−
Group 2: Operative Cases						
16	+	−	+	+	−	+
17	+	−	+	+	−	+
18	+	−	+	+	−	+
19	+	−	+	+	−	+
20	+	−	+	+	+	+
21	+	−	+	+	−	+
22	+	−	+	+	−	+
23	+	+	+	+	−	+
24	+	−	+	+	−	+
25	+	−	+	+	−	+

* Extrapyramidal signs included tremors, dystonia and athetotic movements.

far as can be determined. Since the average interval from first potential exposure to onset of cerebral symptoms in this series was 12.8 weeks for cases in group 1 and 22.8 weeks for cases in group 2, it would seem that the appearance of ova in the stools in cases with localization outside the hepatic portal system is considerably delayed as compared with that in the usual clinical case.[43]

Other parasites present in these cases on routine examination of the stool were: hookworm, 5 cases; Ascaris lumbricoides, 2 cases, and Endamoeba histolytica, 5 cases. In 10 cases no ova or parasites other than S. japonicum were noted, while data on examination of the stools in the remaining 3 cases were incomplete. It is not felt that the

presence of hookworm, ascaris or E. histolytica in the stools of half the patients contributed to the neurologic syndromes seen.[30a]

Data on the spinal fluid obtained on lumbar puncture in the cases reported from 1899 to 1944 are incomplete, but in seven examinations on 4 patients the findings were not of diagnostic significance. In 1 case the reaction of the spinal fluid for globulin was reported as 2 plus and an initial pressure of 310 mm. of water was recorded.

Observations on the spinal fluid were reported from overseas in 13 cases in group 1 of this series. In 5 of these cases (2, 3, 5, 8 and 9) there was mild pleocytosis, with cell counts ranging up to 22 per cubic millimeter in 2 instances. The identity of the cells seen in these initial specimens of fluid is obscure, although in 2 of the 5 cases the cells were specifically designated as lymphocytes. No eosinophils or ova were observed in the spinal fluid of any of the patients in this series,

TABLE 5.—*Data on Hematologic Studies, Lumbar Puncture and Examination of Stools in Twenty-Five Cases of Schistosomiasis of the Central Nervous System in United States Army Personnel*

	Findings at Onset of Cerebral Complications				
			Lumbar Punctures		Interval (Days) from Onset of Cerebral Signs to First Positive Stool (S. Japonicum)*
Case No.	Average Total White Cell, Count	Average Eosinophil Count, %	Number Normal Fluids, %	Number Abnormal Fluids, %	
Group 1 (1-15)	21,000 (range, 12,000-33,000)	49.4 (range, 20-80)	61	39	62 (range, 2-192)
Group 2 (16-25)	12,000 (range, 7,000-16,000)	23.5 (range, 7-65)	67	33	181 (range, 17-380)

* Data exclusive of cases 14 and 25 in which ova appeared in the stools six and eighty-three days respectively, prior to onset of cerebral complications.

either overseas or in the 12 examined here. The only other abnormality noted in the spinal fluids in these cases was of minor nature and consisted in insignificant alteration in the colloidal gold curve in 2 instances.

The spinal fluid was abnormal in two thirds of the operative cases, especially with relation to the initial pressure, the globulin content, the total protein content and the colloidal gold curve. When made, cultures of the spinal fluid in these cases uniformly yielded no growth.

It is possible that more careful examination of the spinal fluid in the early stages may reveal ova or eosinophils. The speed suggested for centrifugation is 500 rotations per minute for thirty seconds (to avoid dissolution of the ova).

The significant data on hematologic studies, lumbar puncture and examination of the stools in these cases are presented in table 5.

Special Studies.—In every case in group 1 (nonoperative) in which roentgenograms were taken of the skull the findings were reported

as within normal limits. Examination of the fundus in these 15 cases also showed a normal condition except in case 1 (transient, mild bilateral papilledema) and in case 2 (chorioretinitis, of the left eye, which lasted for several months).

Roentgenograms of the skull in the operative group showed abnormalities in 50 per cent, the chief finding being a shift of the pineal body to the side opposite the space-occupying intracranial lesion (cases 16 to 18, and 22).

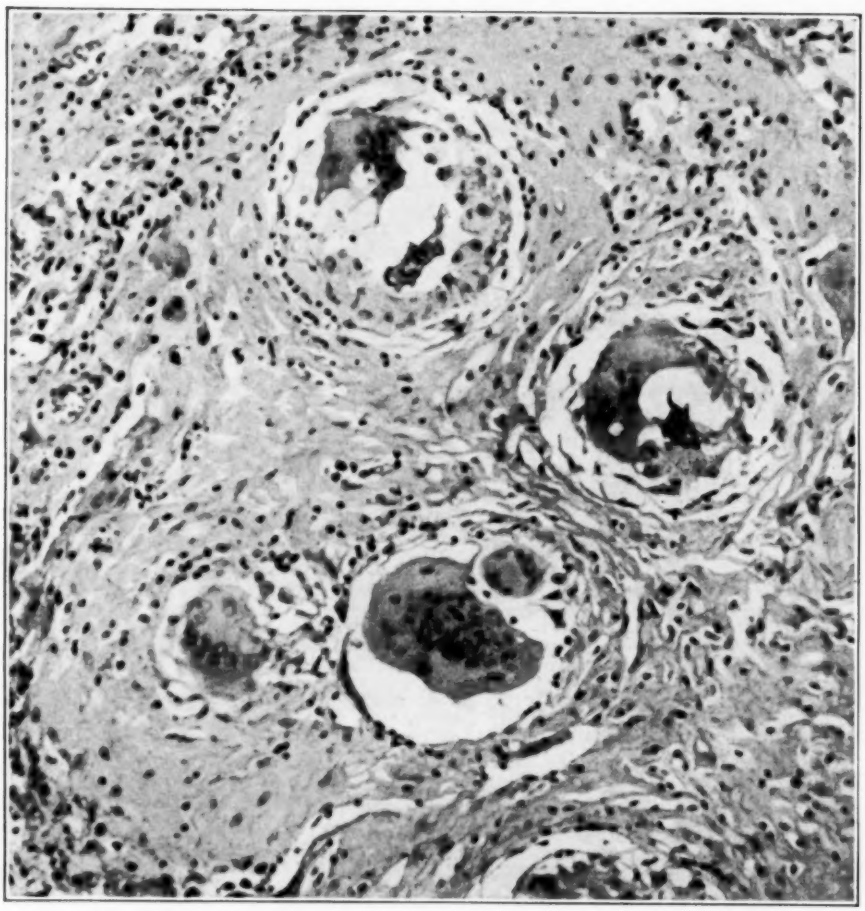

Fig. 5 (case 21).—Section of cortex (× 200), showing nest of ten eggs of S. japonicum. (United States Army Medical Museum negative no. 93460)

Ventriculograms were performed in each instance in group 2, patients with symptoms simulating cerebral tumor. Abnormalities consisting in shift of the ventricular system (lateral and third ventricles) to the side opposite the lesion or defective filling or deformity of one or more ventricles was observed in all but 1 case (23).

Electroencephalography, likewise, was of definite localizing value in this group, since foci of abnormal activity were found to correspond with the main pathologic process in 8 (16 to 22, and 24) out of 10 cases.

Differential Diagnosis.—The most commonly recorded diagnoses on first hospitalization in the group of nonoperative cases were: (*a*) dengue, 3 cases; (*b*) bronchitis or pneumonia, 3 cases, and (*c*) angioneurotic edema, chronic nephritis, encephalitis, battle fatigue, cerebral malaria, hysteria, reactive depression, infectious hepatitis and fever of unknown origin, 1 case each.

In group 2, the preoperative diagnoses were: (*a*) brain tumor, 8 cases; (*b*) subdural hematoma, 1 case; (*c*) cause not specified, 1 case.

The diagnosis of schistosomiasis is based clinically on a careful evaluation of the history and the physical and laboratory findings and is confirmed by the demonstration of ova of S. japonicum in the feces.[45] However, clinical or laboratory findings may not be of great value in establishing the diagnosis of cerebral schistosomiasis, since in 90 per cent of the cases in the present series stools were negative for the ova at the time of onset of cerebral symptoms.

The occurrence of abnormal neurologic findings (especially pyramidal tract syndromes or clinical pictures simulating expanding intracranial lesions) either in proved clinical cases of schistosomiasis or in any case in which the patient has been in an endemic area should make one highly suspicious of involvement of the central nervous system by ova of this trematode. As has been seen, the pathologic process in schistosomiasis japonica has a peculiar predilection for involvement (*a*) of the motor rather than of the sensory tracts and (*b*) of the brain rather than of the spinal cord. Clinically, the symptoms usually appear in the guise of a unilateral or a bilateral pyramidal tract syndrome, although it may simulate encephalitis, meningitis or an expanding intracranial lesion.

PROGNOSIS

The mortality resulting from invasion of the central nervous system by ova of the three human schistosomes has been summarized in table 1.

Only 1 death has been reported in 27 cases of cerebral schistosomiasis japonica observed in World War II. The patient[21] apparently did not die of complications referable to the central nervous system.

On reference to table 6, it is evident that a small percentage of patients in group 1 have made a complete recovery, whereas all patients in group 2 have at present at least minor neurologic residual disturbances. As would be expected, the number of patients with moderate or severe

45. Thomas and Gage.[21] Billings and others.[36a] Most, Kane and others.[37a] Baroody, B. J., and Most, H.: Relative Efficiency of Water Centrifugal Sedimentation and Other Methods of Stool Examination for Diagnosis of Schistosomiasis Japonica, J. Lab. & Clin. Med. **31**:815-823, 1946.

residual disorders has proved to be almost twice as great in group 2 as in group 1. Cerebral schistosomiasis, fortunately, was only rarely a fatal disease, but proved to be disabling for a relatively long time in the majority of cases in which this uncommon complication occurred. Neurologic residual signs were still present a year or more after onset of cerebral complications in 88 per cent of the cases in this series. The neurologic residual disturbances and the extent of clinical recovery in

TABLE 6.—*Summary of Residual Findings at Time of Final Evaluation in Twenty-Five Cases of Schistosomiasis Japonica with Central Nervous System Complications (United States Army Personnel)*

Case No.	Date of Onset of Cerebral Symptoms	From Onset to Final Evaluation *	Residual Findings			
			None	Mild	Moderate	Severe
		Group 1: Nonoperative				
1	7/ 7/45	8 mo.	..	+	..	..
2	1/25/45	13 mo.	..	+	..	..
3	2/ 1/45	15 mo.	..	..	..	+
4	3/ 7/45	11 mo.	+	..	..	..
5	1/ 8/45	14 mo.	..	..	+	..
6	1/29/45	3 mo. (5/1/45)	..	+	..	..
7	2/ 9/45	14 mo.	..	+	..	..
8	1/16/45	15 mo.	..	..	+	..
9	12/25/44	11 mo.	+	..	..	..
10	2/ 1/45	15 mo.	..	..	+	..
11	1/20/45	3 mo. (5/1/45)	..	..	+	..
12	2/15/45	11 mo.	..	..	..	+
13	2/ 9/45	10 mo.	+	..	..	..
14	5/24/45	6 mo.	..	+	..	..
15	3/12/45	7 mo.	..	+	..	..
		Group 2: Operative				
16	6/ 1/44	23 mo.	..	+	..	..
17	5/22/45	11 mo.	..	..	..	+
18	11/ 4/45	6 mo.	..	..	+	..
19	11/11/45	6 mo.	..	..	+	..
20	3/27/45	13 mo.	..	..	+	..
21	3/ 1/45	14 mo.	..	..	+	..
22	1/11/46	3½ mo.	..	..	+	..
23	6/ 6/44	23 mo.	..	..	..	+
24	1/20/45	13 mo.	..	+	..	..
25	5/17/45	?	..	..	+	..
Totals			3	8	10	4
Percentage			12	32	40	16

* "Final" evaluation as of May 1, 1946, except in cases 6 and 11.

25 reported cases of cerebral schistosomiasis japonica are summarized in table 6.

TREATMENT

Prompt institution of specific treatment for schistosomiasis japonica with intravenous injections of antimony potassium tartrate U. S. P. in total doses of 2.22 Gm. is indicated in any case "on clinical grounds" alone, even though the stools may not contain ova. A satisfactory schedule of treatment consists in the cautious intravenous administration of 8 cc. of a freshly prepared 0.5 per cent solution on the first day, followed by doses of 12, 16, 20, 24 and 28 cc. on alternate days; injections

of the last named amount, representing the maximum single dose, are continued on alternate days until a total of 444 cc. has been given. Cough immediately following an injection, arthralgia and electrocardiographic changes commonly occur during treatment but rarely require interruption or discontinuance of therapy.[37a] This therapy is essential not so much with the expectation that specific therapy will alleviate appreciably the immediate effects of occlusion of cerebral vessels (with the surrounding reaction caused by the ova), but with the idea of preventing further deposition of eggs in the brain or elsewhere by killing the adult worms. Adjuvant therapy may include administration of cerebral vasodilators and antispasmodics, use of sedatives and spinal fluid drainage, as indicated.

Operative intervention can be expected to be of assistance only in relieving symptoms of generalized increased intracranial pressure or in removing a gross focus of irritation. In every case, it should be complemented with an adequate course of specific treatment with antimony potassium tartrate, as previously outlined.[37a]

It is recommended further that patients with neurologic complications be followed, with selected clinical and laboratory observations at regular intervals for at least one year.[37a] Although treatment during the stage of convalescence is entirely symptomatic, periodic examination to determine the activity of the disease will serve to reduce the hazard of further possible localization of ova within the central nervous system.

SUMMARY AND CONCLUSIONS

Involvement of the central nervous system in cases of schistosomiasis is an uncommon complication, but a clinical and pathologic entity, which is due to the presence of the ova of S. mansoni, S. haematobium or S. japonicum within the brain or the spinal cord.

Twenty-four cases of this condition had been reported in a period of fifty-five years prior to the landing of American troops on Leyte, in the Philippines, on Oct. 20, 1944, and these cases are reviewed in the present paper.

Experience obtained during nineteen months of World War II, from Oct. 20, 1944, to May 1, 1946 has made it possible to study an additional 27 cases of schistosomiasis japonica, 17 of which have been under observation at this hospital from three to twelve months during the first year and one-half after onset of abnormalities referable to the central nervous system.

In 22 of these cases, the evidence for the neurologic diagnosis is clinical only, although highly presumptive, there being no mortality in the group. In the remaining 5 cases, the diagnosis rests on firm pathologic grounds, since the characteristic ova were observed in sections taken from the central nervous system at operation.

The diagnosis of schistosomiasis japonica is based on the presence of one or more of the following points: (*a*) a reliable history of exposure to potentially infected fresh water in a known endemic area (China, Japan, Formosa or the Philippines); (*b*) the presence of fever, malaise, generalized aching, cough, headache, anorexia, nausea, vomiting, diarrhea, progressive loss of weight, urticaria or angioneurotic edema with abdominal tenderness and enlargement of the liver; (*c*) the observation of leukocytosis, with a high eosinophil count in the peripheral blood smear, and characteristic sigmoidoscopic findings.

Involvement of the central nervous system is manifested by a more or less sudden onset of paralysis or weakness of one or more extremities, diffuse encephalitic signs or focal epileptic attacks.

Pathologically, the lesions of schistosomiasis are due almost entirely to the presence of the ova of the trematodes, which in the case of S. japonicum show a remarkable predilection for localization within the brain (cortex, subcortex, internal capsule and basal ganglia), and in the case of S. mansoni and S. haematobium have been reported to localize only in the spinal cord.

Microscopically, the pathologic process is one of intense reaction around the ova, with edema, necrosis, cellular infiltration (including foreign body giant cells), phlebitic changes and degeneration of the surrounding neural parenchyma.

Careful and repeated examinations of the stools are important in establishing the clinical diagnosis, but specific treatment should not be delayed if there is adequate presumptive evidence for the diagnosis, even though all examinations of the stool may be negative for the ova up to the time of onset of abnormalities of the central nervous system.

Examination of the spinal fluid has not proved of diagnostic significance except in cases with symptoms suggestive of an expanding intracranial process in which increased cell counts and abnormal values for the total protein are commonly found.

The chief neurologic features of these cases are as follows: (*a*) with S. mansoni and S. haematobium, syndromes mainly of spinal cord origin, i. e., transverse myelitis; and (*b*) with S. japonicum, (1) monoplegias, hemiplegias or quadriplegias of cortical, subcortical or capsular origin; (2) diffuse encephalitis and/or meningitis, and (3) syndromes simulating tumor of the brain.

Operative intervention may be indicated in cases with focal epileptic seizures, and prompt institution of adequate specific treatment (intravenous injection of 2.22 Gm. (total) of antimony potassium tartrate U.S.P.) is recommended in all cases in order to prevent further localization of ova within the central nervous system.

The immediate prognosis for life in cases of this condition is good, but mild to severe neurologic residual disturbances may be expected in a significant proportion of cases for at least one year after the time of onset.

Further cases may occur in occupation troops stationed in the Far East or among veterans who have served in endemic areas.

Cerebral schistosomiasis will continue to demand a high degree of clinical awareness, since it may appear not only in cases in which there is a definite history of schistosomiasis but in any case in which there has been exposure to the infection, even after a "silent" or latent phase, which may be as long as two to four years.

APPENDIX

The 27 cases of cerebral schistosomiasis japonica observed among American Army personnel in World War II may be classified as follows:

Case No.	
(*a*) 1-4; 16..... Total.....5	Not previously reported elsewhere; observed at Moore General Hospital
(*b*) 24..... Total.....1	Not previously reported elsewhere and not observed at Moore General Hospital
(*c*) 5; 7-10; 12-15; 17-19 Total.....12	Previously reported elsewhere (see below) with follow-up observations at Moore General Hospital

Case No.	Author
5; 7-10.....	Tillman [23]
12-15.....	Carroll [24]
17.....	Watson and others [25]
18 and 19.....	Maltby and Schmidt [26]

Total cases seen at Moore General Hospital (17)

Case No.	
(*d*) 6; 11; 20-23; 25; 26; 27	Previously reported elsewhere (see below) and not seen at Moore General Hospital (9)

Case No.	Author
6; 11.....	Tillman [23]
20; 23.....	Spiegel [27a]
21; 22.....	Uihlein and Perkins [27b]
25.....	Carroll [24]
26; 27.....	Thomas and Gage [21]

Total of all reported cases (27)

Clinical abstracts of representative cases observed at Moore General Hospital are presented here. Two of these (cases 2 and 16) have not been reported elsewhere.

CASE 2.—Flaccid left hemiparesis; chorioretinitis.

A 27 year old soldier in the armored force arrived on Leyte on Nov. 23, 1944 and remained there for three months. For about six weeks, from Dec. 1, 1944 to Jan. 10, 1945, he was exposed to infected fresh water by wading in swamps and rice paddies.

Past and Family Histories.—He stated that he had "rheumatism" at the age of 12 and that at 18 he was hospitalized briefly for "Bright's disease."

Course of Illness.—About January 8, six weeks after the first potential exposure, he noticed insidious onset of malaise, headache, anorexia and weakness. Five

for the next four days. At about the same time he had intermittent low grade fever, which lasted approximately one week. On January 14 "giant hives" suddenly appeared on the upper part of his trunk.

He was first hospitalized on January 21 at a United States Army station hospital overseas, where physical examination on admission showed that he was acutely ill, with swelling around both eyes and urticaria about the waist and the upper part of the trunk. His condition remained essentially unchanged until January 27, when sudden loss of consciousness, followed by peculiar behavior, apathy and incontinence, pointed to cerebral involvement (eight weeks after the first exposure). Neurologic examination revealed intense restlessness and hyperactive tendon reflexes, with bilateral ankle clonus and Babinski and confirmatory signs. There were no signs of meningeal irritation. Shortly thereafter he was transferred to a United States Army general hospital overseas. On January 29 lumbar puncture revealed 22 cells per cubic millimeter, 19 of which were considered to be lymphocytes. The spinal fluid was not otherwise remarkable. On January 21 he emerged from the semistuporous condition of the preceding seventy-two hours and complained of inability to move his left arm and leg. Pronounced eosinophilia (8,000 to 14,000 white cells with 36 to 52 per cent eosinophils) was found. Despite negative results in fifteen examinations of the stools for ova and parasites, he was given three courses of emetine hydrochloride (total dose, 17 grains 1.1 Gm.) from February 9 to March 12 for schistosomiasis on clinical grounds, with little or no change in his general condition.

An interesting feature of this case was the discovery on January 29 of an unusual lesion in the left fundus, which was described in detail by three consultants. They expressed the belief that it was unique. Vision under homatropine cycloplegia was 20/30 in the right eye and 20/50 in the left eye on February 9. The lesion was described as a "billowy white mass, which measured 1 by ½ disk diameter,[46] was triangular and lay in the fork made by branches of the inferior temporal vein, with edema of the surrounding retina. It did not resemble a recent hemorrhage or exudate, and there were no opacities in the vitreous. Over a period of several weeks this bizarre lesion was kept under careful observation and was seen to recede slowly, but on March 14 it was still present and was associated with blurring of the inferior margin of the left optic disk. The ophthalmologic diagnosis was "acute chorioretinitis in the left eye, of unknown cause, perhaps parasitic." On Feb. 26, 1945, vision was 20/15 in the right eye and 20/30 in the left eye, and on March 20 vision in the left eye was completely normal (i. e., 20/20).

Observations at General Hospital.—On May 9, three and one-half months after onset of his cerebral complications, he was admitted to Moore General Hospital, complaining of weakness of the left arm and leg. General physical examination revealed nothing remarkable. He was approximately 10 pounds (4.5 Kg.) underweight. Neurologic examination revealed weakness and "clumsiness" of the left arm and weakness of the left leg, especially of the hamstring muscles. The cranial nerves were intact. No sensory changes were found. The tendon reflexes were hyperactive, especially on the left, but no abnormal reflexes were elicited. The superficial reflexes were present bilaterally and were equal on the two sides. The lesion in the fundus of the left eye previously described was not visualized on careful examination. The patient appeared to be a tense, "nervous" person and complained of inability to remember things. There was no other disturbance of the sensorium or any defect of speech or gait, tremor or ataxia.

46. Approximately 1,500 by 750 microns. The average dimensions of ova of S. japonicum are 90 by 65 microns (Faust and Melency,[1] page 15).

After two negative stools, ova of S. japonicum were discovered for the first time on May 26 and 29 (four months after onset of complications referable to the central nervous system). Hematologic studies on admission showed nothing remarkable except for a count of 14 per cent eosinophils. Examination of the spinal fluid revealed 5 lymphocytes per cubic millimeter, 27 mg. of protein per hundred cubic centimeters, a negative reaction for globulin, a negative Wassermann reaction and a normal colloidal gold curve in all dilutions. No ova or eosinophils were observed in the fluid. A roentgenogram of the chest showed nothing abnormal.

Specific treatment for schistosomiasis was promptly started, and the patient received 70 cc. of stibophen intramuscularly from May 28 to June 25, without appreciable toxicity. One hundred and ten days later (October 6) viable ova of S. japonicum were again found in his stools, and he was again treated with a full course of intravenous injections of antimony potassium tartrate U. S. P. (2.08 Gm. from October 7 to November 8). This treatment was complicated by mild gastrointestinal distress during the last week of injections. Little improvement in his neurologic status was evident at the end of either course of therapy. However, on his return from furlough, he stated that the strength of his left arm had improved somewhat but that the weakness of his left leg was essentially unchanged. Neurologic examination on Jan. 23, 1946 revealed hyperactivity of the tendon reflexes on the left, with sustained ankle clonus on the left side, but no abnormal reflexes. There was distinct impairment, though relatively mild, of rapid movements of the fingers of the left hand and forearm. Vision, including the visual fields, was normal in both eyes. On Jan. 23, 1946, the ophthalmologist at this hospital reported "indistinctness of the inferior nasal margin of the left optic disk" without elevation. Vision in the eye was 20/20, with no evidence of a central scotoma.

On March 1, thirteen months after the onset of cerebral complications, the patient was discharged to his own care. Neurologic examination just prior to discharge revealed minimal left hemiparesis, which was more noticeable in the upper than in the lower extremity.

Comment.—The case is characterized by insidious onset of schistosomiasis six weeks after the first potential exposure and sudden onset of signs referable to the central nervous system two weeks later, with signs of a diffuse encephalitic process and focal lesions, the latter affecting the right internal capsule predominantly. The bizarre lesion noted in the left fundus in this case is a unique complication of schistosomiasis and may have been due to the presence of a schistosome egg, with surrounding area of reaction.

Prognosis.—The prognosis is fairly good. The patient still has mild residual left hemiparesis with some slowing of the mental reactions. The latter cannot be expected to improve significantly from this point, since it has been over a year from the time of onset of cerebral complications.

CASE 8.—Spastic quadriplegia; meningeal signs; involvement of the cerebellum and cranial nerves.[23]

A cannoneer aged 28, white, landed on Leyte on Oct. 23, 1944. The clinical onset was eight weeks after the first potential exposure and was manifested by low grade fever, watery diarrhea and abdominal cramps. There was sudden onset of symptoms referable to the central nervous system eleven weeks after the first exposure with diffuse encephalitic and meningeal signs, together with focal lesions probably involving both internal capsules, the brain stem and the cerebellum with resulting spastic quadriplegia. The third, seventh and ninth cranial nerves were at least transiently affected. All the stools examined overseas were negative for ova of S. japonicum. Treatment overseas consisted in administration of 80 cc. of

stibophen intramuscularly, starting Jan. 29, 1945; slight improvement resulted.

Subsequent Observations.—On June 8, five months after onset of complications referable to the central nervous system, the patient was admitted to Moore General Hospital complaining of weakness of the legs, unsteadiness on walking, moderate nervousness and slight defects in speech (hesitancy) and recent memory. He appeared chronically ill and at least 10 years older than his stated age; yet he was alert, well oriented and cooperative. Neurologic examination revealed that the cranial nerves were intact; there was weakness of all the extremities with slight spasticity (severer in the legs than in the arms); the tendon reflexes were hyperactive in the lower limbs, with unsustained ankle clonus and an equivocal extensor plantar response on the right side. Superficial reflexes were absent bilaterally. There was some past pointing on the right with mild intention tremor, but no nystagmus, dysmetria or adiadokokinesis could be made out. No sensory defects were found. The visual fields and the optic fundi were normal.

Laboratory Findings and Subsequent Course.—Examination on admission revealed a white blood cell count of 10,700 with 6 per cent eosinophils. His stools continued to be negative for the ova of S. japonica until July 8, 1945, when three successive specimens were found to be positive (twenty-five weeks after onset of symptoms of involvement of the central nervous system). On July 12 treatment was started with a course of intravenous injections of antimony potassium tartrate, and he received a total of 1.80 Gm., finishing the course on August 9. His neurologic status remained essentially unchanged throughout treatment. On return from a thirty day furlough, he reported a gain in weight of 15 pounds (6.8 Kg.), and definite improvement had taken place in his speech and gait. Two months after the end of treatment his abdominal reflexes were present, and there was inequality of tendon jerks on the two sides (those on the right were stronger than those on the left). Four months after treatment little additional improvement had occurred in his general condition. On Feb. 1, 1946, about one hundred and seventy-five days since the last day of treatment with antimony potassium tartrate, viable ova of S. japonicum were again found in the stools, and the patient was again treated with 100 cc. of stibophen given intramuscularly from February 7 to February 20. After return from a convalescent furlough, he seemed much improved, had gained about 8 pounds (3.6 Kg.) and noted that his legs were stronger. The neurologic findings were unchanged, however. At the time of writing (May 1, 1946), about fifteen months from the date of onset of abnormalities referable to the central nervous system, the patient is still under observation at this hospital, but is ambulatory and not greatly incapacitated by the spastic weakness of his lower extremities.

Prognosis.—The outlook is fairly good. Specific treatment was started two weeks after the date of onset of cerebral symptoms. Response to the first course of 80 cc. of stibophen was practically negligible, but rapid, sustained response was noted to the second course, consisting of administration of 100 cc. of the drug.

CASE 12.—Right hemiparesis; organic psychosis (?).[24]

A white officer aged 21 was first exposed to infected fresh water on Leyte about Dec. 6, 1944. The clinical onset occurred about six weeks later, and onset of symptoms of involvement of the central nervous system, two weeks thereafter, when there developed a severe disturbance of the sensorium, probably due to diffuse encephalitis, followed by signs of early focal lesions in the internal capsule on the left side and, later, evidence of bilateral involvement of the pyramidal tracts. Eggs of S. japonicum were first observed in the stool three days after onset of cerebral symptoms, on Feb. 6, 1945. Treatment overseas consisted in adminis-

tration of 40 cc. of stibophen. No significant improvement was noted until after about 20 cc. had been given; his neurologic status remained essentially unchanged up to the time of evacuation.

Subsequent Observations.—On April 14, 1945, he was evacuated by air to the United States. On admission to Moore General Hospital, on May 5, two and one-half months after the onset of difficulties referable to the central nervous system, he complained of generalized weakness, easy fatigability, headaches and "tingling in the head." In addition, he admitted having experienced numerous auditory hallucinations. The findings on general physical examination were within normal limits. Neurologic examination showed no disturbance of speech or gait. The cranial nerves were intact, and the optic fundi were normal. No sensory defects were found. There was no evidence of weakness, muscular atrophy or altered tonus on the right side. However, all the tendon reflexes were hyperactive, and there were bilateral, unsustained knee and ankle clonus. No abnormal reflexes were elicited. All the superficial reflexes were diminished. His mental status fluctuated considerably, but there was a definite loss of memory with intermittent periods of confusion and disorientation, together with auditory hallucinations.

Laboratory Findings.—The hemogram showed 4,700,000 red blood cells, 91 per cent hemoglobin and a white cell count of 11,800 with 23 per cent eosinophils. The stools were persistently negative for all ova and parasites during this hospitalization.

Treatment and Subsequent Course.—On May 16 proctoscopic examination revealed low grade inflammation of the mucosa of the rectosigmoid portion. Despite the absence of ova in the stools, he was given a course of 70 cc. of stibophen intramuscularly, completing the treatments on June 22. Two weeks later (July 14) he turned in at a station hospital in Indiana in an agitated state. He claimed he had "a mission to perform," that people were talking about him, that he was brilliant and had a close relationship to God. The diagnosis of "psychosis, schizophrenia" was reached, and he was transferred to Billings General Hospital on July 17. He was extremely restless and excited and had ideas of reference, delusions and feelings of unreality. The diagnosis at that hospital was "psychosis, unclassified" and he was transferred back to Moore General Hospital.

On his second admission, on August 7, he complained of occipital headaches and auditory hallucinations and seemed extremely agitated. Neurologic findings revealed hyperactive tendon reflexes throughout, with ankle clonus and a plantar response of extensor type on the right. He was seen by a psychiatrist, who noted "bizarre ideation, confusion, lack of insight and judgment." Speech was hesitant. There was no evidence of intellectual deterioration. A roentgenogram of the skull revealed no abnormality, and lumbar puncture, on August 10, showed a normal status. He was given a second course of treatments for schistosomiasis, consisting in intravenous injections of 1.80 Gm. of antimony potassium tartrate from August 20 to September 18, without appreciable side effects. In addition, he received individual psychotherapy, dehydration and subshock insulin therapy. There was little definite change in his mental status, although "at times he seemed to show improvement." At no time in this hospital was the course of the disease febrile.

On October 31, six weeks after the end of his second course of treatments, there was no appreciable alteration either in his neurologic or in his mental status; i. e., there was still strong evidence of bilateral involvement of the pyramidal tracts and disturbance of personality. On November 2, six and one-half months after the onset of his cerebral difficulties, he was transferred to a neurosurgical center

for further observation, with the recommendation that ventriculography and electroencephalography be considered as diagnostic aids.

Examinations by members of the neurologic section there revealed only "generalized hyperreflexia," and it was felt that there was "no organic basis for his psychosis." A diagnosis of "dementia precox, paranoid type" was reached, and he was transferred to another general hospital for further observation and care. A recent neurologic examination emphasized the masklike facies and the hyperreflexia of the lower extremities, more pronounced on the right than on the left. Slight improvement in insight and judgment has been noted. The final diagnosis at this installation was "psychosis, with associated structural changes in the brain."

Prognosis.—The prognosis is not clear. The patient's family and past histories reveal no known neuropsychiatric background. The mental symptoms in this case were prominent from onset, but, unlike those in the other cases, have persisted without significant amelioration. While organic psychosis on the basis of structural changes in the brain due to parasitic infection is rare, it has been reported,[47] and, although the mechanism varies with the species of parasite, must be considered at least a plausible explanation in this case. Since the first effective treatment for schistosomiasis which the patient received came almost four months after the onset of cerebral manifestations, his failure to respond in the usual manner cannot definitely rule out the possibility of a widespread encephalitic process, possibly with maximum concentration of ova in the frontal lobes. The prognosis in this case is still *sub judice*.

CASE 15.—Flaccid monoplegia; acute cardiac failure.[24]

A white soldier aged 21 was exposed to infected fresh water on Leyte for three weeks, from Nov. 24 to Dec. 12, 1944. Gradual onset of clinical symptoms occurred seventeen weeks from the date of the first exposure. Symptoms of cerebral involvement appeared suddenly six weeks later, with pronounced disturbance of the sensorium and subsequent development of flaccid monoplegia of the left upper extremity. The original pathologic process in this case was undoubtedly diffuse encephalitis, with an additional focal lesion close to the motor cortex on the right side. The ova of S. japonicum were first observed in the stool one week after onset of the cerebral complications. Treatment overseas consisted in administration of 60 cc. of stibophen in two weeks, beginning May 14 the day of onset of cerebral manifestations of the disease. Eight days after the completion of treatment the patient had an acute episode of cardiac failure, which was thought to be "rheumatic" in origin.

Subsequent Observations.—On August 8, three months from the date of onset of his first cerebral symptoms, he was admitted to Moore General Hospital, complaining only of weakness of grip in the left hand. Physical examination revealed a well developed and well nourished white man, in no acute distress. Examination of the chest showed enlargement of the area of cardiac dulness, both to the right and to the left; accentuation of the pulmonic second sound, and a blowing mitral systolic murmur, with regular rhythm. Neither the liver nor the spleen could be palpated. Neurologic examination revealed slight but definite weakness (apraxia) of the left arm, most evident in the distal muscles, without evidence of flaccidity, atrophy, spasticity or altered tonus. The tendon reflexes were somewhat more active on the left than on the right, but no abnormal reflexes were present and the superficial reflexes were active and equal on the two sides. The cranial nerves, fundi, sensory status and mental status were within normal limits.

47. Masson, C. B.: Effects of Malaria on the Nervous System with Special Reference to Malarial Psychoses, Am. J. M. Sc. **168**:334-371, 1924. von Henneberg.[30c]

Laboratory Findings.—A complete blood count revealed nothing abnormal. Twenty-four specimens of stools were negative for all ova and parasites. Lumbar puncture revealed a completely normal status except for a 1 plus reaction for globulin; no eosinophils or ova were seen.

Subsequent Course.—The patient's stay in the hospital was uneventful. A roentgenogram of the heart (taken at a distance of 7 feet) on August 18 revealed a cardiothoracic ratio of 13.5:28 (upper limit of normal), with no "no dilatation of any chamber" An electrocardiogram showed abnormal P waves (diphasic in leads I, II and III), but the P R interval was 0.12 second. Erythrocytic sedimentation rates on August 9 and November 15 were normal. No specific treatment for schistosomiasis was given. On November 30, six and one half months after the onset of cerebral manifestations and three and one half months after his admission, he was discharged with minimal residual paresis of the left arm.

Prognosis.—The outlook in this case is good. An immediate response to specific treatment was noted, and the patient subsequently made a virtually complete recovery. There is no subjective cardiac disability at present, but electrocardiographic abnormalities were present at his discharge.

In the light of evidence that ova may occasionally be observed in the myocardium,[10] it is interesting to speculate on the possibility that the acute cardiac failure complicating his illness might have been schistosomal or schistosomal and toxic, i. e., precipitated by treatment with a heavy metal.

CASE 16.—Space-occupying lesion in the parieto-occipital region of the left cerebral hemisphere; secondary focus involving the right motor area of the cortex (?).

A white officer aged 26 was forty-two months overseas in the Pacific area, thirty-two of which were spent as a prisoner of the Japanese, mostly in the Davao Penal Colony on Mindanao, P. I.

The past and family histories revealed no known neuropsychiatric background.

After the defeat of the United States forces on Corregidor, he escaped to Mindanao and managed to elude the Japanese until May 1942. During this time, his outfit was in central Mindanao, and the men often swam in fresh water streams and lakes in that area. Since he was never on Leyte, it is reasonably certain that he contracted the infection on Mindanao. In addition to schistosomiasis, he suffered from repeated attacks of malaria; he had pellagra and beriberi with peripheral neuritis in March 1943 and severe "nutritional" edema early in 1944. The maximum loss of weight was 45 pounds (20.4 Kg:).

It is difficult to date the period of actual exposure to infected fresh water, but he recalled that he worked in rice paddies almost daily during the latter part of 1943. During December of the same year he had an episode of severe bloody diarrhea, which lasted about two weeks and left him in a weakened condition. This subsided spontaneously, and he had no further symptoms referable to schistosomiasis until the onset of cerebral complications following relatively minor head trauma in a prison camp near Davao on June 1, six months later. He was unconscious for "about twelve hours" and in a semistupor for another ten days. No further symptoms referable to the nervous system occurred until October 1944, when he suddenly became incoherent while working under a hot sun. A generalized convulsion ensued, with unconsciousness and biting of the tongue. After the first convulsion, he had generalized seizures, associated with dizziness, left-sided headaches, blurring of vision and weakness of the left arm, at intervals of about one month up to the time he was repatriated at Camp Cabanatuan on Luzon, on Jan. 31, 1945. On several occasions in the interim he had a low grade fever, known as "colon fever." After brief processing at an evacuation hospital and replacement

center, he was evacuated by ship to the United States with the diagnosis of "post-traumatic syndrome." Two minor seizures occurred en route, during the second week of February, and were followed by a period of confusion, lasting ten to twelve hours and accompanied with blurring of vision in the right half of the visual field.

Soon after arriving in this country, he was transferred to Cushing General Hospital, Framingham, Mass. On admission there (March 17), nine months after onset of signs referable to the central nervous system he complained of constant haziness, repeated headaches, convulsions, weakness and clumsiness of the left arm, blurring of the right half of the visual field, dizziness and bilateral tinnitus with deafness in the right ear. General physical examination revealed mild generalized furunculosis and minimal pitting edema of the ankles. Neurologic examination revealed slight hesitancy in speech, slowing of mental reactions, amimia involving the right side of the face, diminution in hearing in the right ear and a defect in the right visual field (right inferior quadrant defect as shown with the tangent screen) with bilateral scotoma. A neurologic consultant could find no evidence of motor dysfunction in the left hand one month after admission. The reflexes seemed to be increased on the right.

Laboratory Findings.—Mild anemia (3,900,000 red cells, with 12.9 Gm. of hemoglobin) was found on admission. The total white blood cell count was 14,100, with 8 per cent eosinophils. Spinal punctures repeatedly showed a normal condition of the fluid except for an increased total protein content (55 to 73 mg. per hundred cubic centimeters) and slightly abnormal initial pressures. Multiple hepatic function tests gave values within normal limits. Ova of S. japonicum were observed in the stools on April 4, and on seventeen other occasions, until May 31, 1945.

Special Studies and Operative Measures.—Hearing acuity was reported to be diminished to 5/15 on the right (normal on the left). Sigmoidoscopic examination revealed nothing abnormal. A number of electroencephalographic tracings were made, all indicating cerebral dysrhythmia, which was most prominent in the left parieto-occipital region of the brain. Roentgenograms of the chest and skull were normal. Ventriculograms showed a normal condition except for incomplete filling of the left temporal horn. Up to April 2, when the first operation was carried out (two days before ova of S. japonicum were found in the stools), the tentative diagnosis was "subdural hematoma." Burr holes were made in each parieto-occipital region of the skull, but no blood clot was encountered. Another burr hole was made in the left temporal region of the skull, and "resistance" was noted on palpation several centimeters below the surface of the cortex. The wounds were closed, and further surgical procedure was delayed indefinitely, since the patient continued to improve spontaneously.

Subsequent Observations.—He was seen in consultation by Dr. L. E. Napier, of the Harvard Medical School, who recommended that he be given two courses of stibophen, of 55 cc. each. On completion of the second course of treatment, on July 1, the right visual field defect had largely disappeared; his hearing had improved, but he still complained of impairment of the higher intellectual functions. This loss was found to be minimal when checked by psychometric testing on August 24. The rest of his stay at Cushing General Hospital was uneventful, and on September 11 he was discharged to a convalescent center prior to final disposition. Between this date and his admission to the Moore General Hospital, on Jan. 16, 1946, the patient had been in two AAF convalescent hospitals and was about to be retired when it was decided to transfer him to a tropical disease center

for final evaluation, although all laboratory studies had failed to reveal parasitic infection.

On admission to this hospital, he still complained of inability to concentrate, especially when tired, and of occasional haziness of vision on the right. General physical examination revealed nothing remarkable. Examination of the skull revealed that the operative wounds had healed well and that there was no tenderness of the scars. All the cranial nerves appeared normal to testing. There were no demonstrable localizing sensory or motor signs; all tendon and superficial reflexes were present and were equal and active on the two sides. There were a slight tendency to "grope" for words and some hesitancy of thought, but no other evidence of intellectual deterioration or personality changes was found. Special examinations of the visual fields showed that they were entirely normal. Although there was no leukocytosis or eosinophilia on the patient's admission, the cutaneous test gave a positive reaction for schistosomiasis [48] and viable ova of S. japonicum were found on Jan. 21 and 22, 1946.

Treatment was then promptly started, and he received 100 cc. of stibophen intramuscularly from January 24 to February 8. Moderately severe nausea and vomiting began about midway in the course and required two rest periods of twenty-four hours each and parenteral administration of fluids, but subsided promptly when administration of the drug was discontinued.

At the time of writing (May 1, 1946), almost two years from the onset of cerebral complications and three and one-half months from the time of his admission to this hospital, the patient is still under observation here. The neurologic status is unchanged; i. e., there are no localizing signs, but he still complains of inability to "concentrate" or to remember things which occurred in the recent past.[49]

Comment.—Infection in this case was undoubtedly contracted on Mindanao, in the Philippines, after prolonged exposure, possibly over a period of two years. The clinical onset is hard to date, but signs of involvement of the central nervous system appeared six months after an episode of diarrhea, in December 1943. The patient had repeated convulsions on the left side together with a speech difficulty and a defect of the right visual field, indications of bilateral intracranial processes. With the aid of special diagnostic studies, these signs pointed to a space-occupying lesion in the parieto-occipital region of the left cerebral hemisphere, with a possible secondary focus involving the right cortical motor area. Cranial operation was performed because of suspected subdural hematoma, but material was not obtained for biopsy. Ova of S. japonicum were found in the stools two days later. Recovery of mental functions actually began before specific treatment was begun, but was definitely accelerated by stibophen.

Prognosis.—The prognosis is guarded. Unquestionably, the patient received a much heavier initial infection than any of the men whose cases have previously been presented.

CASE 17.—Intracranial space-occupying lesion in the left parietotemporal lobe.[25]

An infantryman aged 30, white, was first exposed to infected fresh water on Leyte on about Nov. 15, 1944. The clinical onset was gradual, with remittent low grade fever, anorexia, nonproductive cough, abdominal cramps and diarrhea, the symptoms beginning about two weeks after the first potential exposure. On May

48. Cercarial antigen derived from S. mansoni was given by intradermal injection in a 1:5,000 dilution. The reaction was read after ten minutes against that in a control test with isotonic solution of sodium chloride. A positive result is any difference of 4 mm. in the diameter of the two wheals.

49. The same complaints persisted as of Oct. 1, 1946, despite a second course of treatment (2.22 Gm. of antimony potassium tartrate) from June 7 to July 11, 1946.

22, he had his first episode of unconsciousness, without a convulsion, followed by transitory dysarthria. Repeated grand mal and psychomotor seizures and occasional right sided jacksonian seizures occurred prior to his evacuation to the United States, on June 12. No localizing neurologic signs were elicited on repeated examinations overseas. The white blood cell count was 16,300 with 65 per cent eosinophils on April 6, 1946, when ova of S. japonicum were observed in the stools, and 11,900 with 20 per cent eosinophils at the time of onset of cerebral symptoms. The only treatment he received overseas consisted in administration of 10 grains (0.65 Gm.) of emetine hydrochloride between April 6 and April 18, to which there was little or no response in the gastrointestinal symptoms. Sedation with phenobarbital and diphenylhydantoin sodium (0.2 Gm. daily) was also given after the first seizure.

Subsequent Observations.—On June 24 the patient was admitted to the O'Reilly General Hospital, Springfield, Mo., approximately six and one-half months after exposure and one month after the onset of cerebral complications. The family and past histories were considered noncontributory. General physical examination showed evidence of emaciation, with the liver palpable 4 cm. below the right costal margin. Neurologic examination revealed that the gait was superficially cerebellar in type. There was no evidence of motor weakness, altered or abnormal reflexes, sensory loss or abnormalities of the cranial nerves. In addition, the optic fundi and visual fields were observed to be normal.

Operative Treatment.—After preoperative studies, the first of two craniotomies was carried out on July 5. This consisted in subtemporal decompression on the left side. Biopsy of a mass in the left parietotemporal region, a section of which was stained with hematoxylin and eosin, revealed a granulomatous process surrounding "doubly refractile, light brown paraboloid structures, measuring 60 by 40 microns," i.e., immature ova of S. japonicum. This observation was confirmed by pathologists at the Army Medical Museum. No attempt was made to remove the mass *in toto*. After operation, treatment with diphenylhydantoin was continued as before, and a course of 75 cc. of stibophen was given intramuscularly. After this, the eosinophil count gradually receded, but seizures continued despite heavy sedation (diphenylhydantoin sodium, 0.9 Gm. daily). Because of this and the persistence of prominent electroencephalographic changes, a second craniotomy was performed on November 5, when it was seen that the mass in the region of the angular gyrus had receded. A partial resection of scar tissue was completed, and ova were again demonstrated without difficulty. The patient did well for a short time after operation, but the seizures recurred despite medication with diphenylhydantoin and phenobarbital. When it seemed unlikely that there was any further danger of an acute neurosurgical emergency, the patient was transferred to the Moore General Hospital for further specific treatment of schistosomiasis, arriving on Jan. 10, 1946, approximately seven months after onset of cerebral symptoms.

Subsequent Observations.—On admission to Moore General Hospital, the patient complained of recurrent "spells of uncontrollable crying," left-sided headaches and "poor memory," by which he meant inability to concentrate for more than a short time.

Physical Examination.—A bony defect 2 cm. in diameter was situated above and anterior to the left ear. Except for evidence of moderate emaciation, the physical status was normal.

Neurologic examination revealed generalized weakness with atrophy of disuse of the muscles of the lower extremities. There was some diminution of strength in the right hand grip. The patient could not stand without support and was ataxic on walking. Cranial nerve, sensory, reflex or other neurologic abnormali-

lies were absent. The optic fundi were normal, and no visual defect could be demonstrated either on gross confrontation or by perimetric tests. Psychiatric examination revealed good intellectual endowment, dubious insight and definite inability to master abstract thinking or to retain the content of material examined more than five minutes previously. There was no true break with reality, however.

Laboratory Studies.—The complete blood count was normal on admission except for 12 per cent eosinophils. A cutaneous test (cercarial antigen) for schistosomiasis gave a positive reaction.

Treatment and Subsequent Course.—Although ova were not observed in the stools it was decided to treat this patient with antimony potassium tartrate, and he was given a full course of 2.08 Gm. from Jan. 17 through Feb. 18, 1946, without significant side effects. In addition, 0.6 Gm. of diphenylhydantoin sodium and 0.2 Gm. of phenobarbital were given daily from the day after admission. On this schedule he had continued seizures, mostly "crying jags," of mild type, but an occasional episode of grand mal. Because of beginning gingival hyperplasia and continued poor appetite while he was taking this amount of diphenylhydantoin, oral administration of glutamic acid [50] was begun, in a dose of 5 Gm. three times daily with meals (dissolved in fruit juices), and the diphenylhydantoin sodium was gradually reduced to 2 capsules daily (over a period of two months). With this therapy, there was definite diminution both in the number and in the severity of his psychomotor seizures as compared with a control period; what is more important, his appetite increased and he continued to gain weight slowly. He had, however, had one minor grand mal seizure, which responded promptly to intravenous injection of hypertonic solution of dextrose. At present (May 1, 1946) his neurologic status is unchanged, but during the past month he has been relatively free of seizures. After further observation and, possibly, a second course of treatments with antimony potassium tartrate, it is anticipated that this patient will be given a medical discharge and transferred to a veterans' hospital near his home.[51]

Prognosis.—The prognosis is fair. Although there is evidence that the space-occupying-lesion in the left parietotemporal region has definitely receded after two neurosurgical procedures and specific treatment, the patient is still subject to recurrent psychomotor seizures, which are fairly well controlled as long as he remains under treatment with diphenylhydantoin and glutamic acid. A limited amount of additional improvement is to be anticipated in this case.

Col. J. E. Ash, Medical Corps, United States Army, Director of the Army Institute of Pathology, Washington, D. C., furnished the photomicrographs which appear in this paper.

Major Lent C. Johnson, Medical Corps, Army of the United States, chief of laboratory, Mayo General Hospital, Galesburg, Ill., supplied the data in cases 20 and 23, and Col. Arthur A. Marlow, Medical Corps, Army of the United States, chief of the medical service, and Lieut. Eddy D. Palmer, Medical Corps, Army of the United States, of Ashford General Hospital, W. Va., furnished the clinical summary in case 24.

Mrs. Edith Smith and S/Sgt. Florence A. Hanks, Women's Army Corps, assisted in the preparation of the manuscript.

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50. Waelsch, H., and Price, J. C.: Biochemical Aspects of Glutamic Acid Therapy for Epilepsy, Arch. Neurol. & Psychiat. **51**:393-396 (April) 1944.

51. After a second course of treatments with 2.22 Gm. of antimony potassium tartrate U.S.P. given intravenously during June, 1946, the patient continued to have occasional minor seizures but, over a period of three months, regained his ability to walk unaided and in August 1946 was transferred to a veterans' hospital near his home as a semiambulatory patient.

INSULIN SUBSHOCK (SUBCOMA) TREATMENT OF PSYCHOSES AND PSYCHONEUROSES

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THE VALUE of insulin in treatment of certain mental diseases has been proved beyond doubt, even though a long term evaluation of the results suggests that the therapeutic effects are better in the way of producing remissions than actual cures. Most experiences recorded in the medical literature have to do with insulin shock rather than with subshock or subcoma technic. A number of investigators [1] have shown that with insulin shock treatment the rate of remission is from three to five times the so-called spontaneous rate of remission and that the rate of prolonged remission is about twice the rate of prolonged spontaneous remission. During the first years of insulin shock therapy it was hoped that the apparent recoveries would hold for an indefinite period, but subsequent follow-up observations have shown that what had appeared originally to be recoveries were only remissions. These results are further influenced by the duration of illness before treatment is started; patients treated within six months of the onset of clinical symptoms have the highest rate of remission, and the incidence of good therapeutic results gradually decreases, so that after symptoms have been present for two years or more before insulin shock therapy is given the rate is no better than that which might be expected for spontaneous remissions. This observation applies to insulin therapy in which the full shock or the coma technic is used. I found the coma technic too complicated, however, to carry out in an Army general hospital, considering the number of patients needing insulin therapy, the over-all case load of the neuropsychiatric service and the lack of personnel trained in giving insulin therapy by the full shock method. In addition, insulin therapy with the full shock technic was considered impractical, for a medical officer's presence would be required several hours a day and

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1. Bond, E. D., and Rivers, T. D.: Follow-Up in Insulin Shock Therapy, Am. J. Psychiat. **99**:201-202 (Sept.) 1942. Lewis, N. D. C.: Shock Therapy in Mental Disorders: Indications and Value, Connecticut M. J. **8**:218-222 (April) 1944. Gralnick, A.: A Seven-Year Survey of Insulin Treatment in Schizophrenia, Am. J. Psychiat. **101**:449-452 (Jan.) 1945. Insulin Shock Therapy, Study by the Temporary Commission on State Hospital Problems, New York, 1944.

every medical officer had too many neuropsychiatric patients to be able to spare the time. Finally, full insulin shock treatment would require from four to six weeks of active treatment, followed by an additional four weeks of further observation, before the therapeutic results could be evaluated in the individual case and the case then disposed of properly.

The purpose of the present report is to show that insulin treatment given by the intensive subshock technic is effective in producing not only symptomatic improvement but also remission, and perhaps some recoveries, in many of the psychotic patients seen in the Army. In addition, it is shown that the same intensive insulin subshock technic is effective with certain types of severe psychoneuroses.

The etiologic reasons for the effectiveness of insulin, even in subshock doses, are not known, although there are many opinions. From the biophysiologic standpoint, Squires and Tillim [2] expressed the belief that some degree of imbalance of the autonomic nervous system is present uniformly in psychotic patients, particularly those with schizophrenic syndromes, and to a greater degree in patients with acute psychoses. They stated the opinion that insulin hypoglycemia corrected the imbalance of the autonomic nervous system, besides having a sedative value and improving the patient's physical condition to a notable degree. The clinical results which my colleagues and I observed in an Army general hospital suggest that this theory may explain at least part of the therapeutic effect. Another theoretic consideration is stimulation of the carbohydrate metabolism of the brain in response to a transient period of hypoglycemia, with or without some etiologic influence from the associated partial and transient cerebral anoxemia. Stockings [3] divided schizophrenic patients into two groups, depending on their reaction to insulin. One group responds well to insulin; these he termed the dysglycolytic type, which he described clinically as presenting symptoms of overactivity, elation, motor excitement and a great variety of bizarre delusions and hallucinations; their illnesses were clinically diagnosed as acute manias, hebephrenic and catatonic excitements and paraphrenias. The other group, who did not respond to insulin but did react to anoxic shock (electric shock), he termed dysoxic: these patients showed symptoms of depression, retardation and apathy, and their illnesses were clinically diagnosed as psychotic depressions, para-

2. Squires, M., and Tillim, S. J.: Physiologic Concept of Hypoglycemia and Convulsive Therapy, Psychiatric Quart. **18**:92-104 (Jan.) 1944.

3. Stockings, G. T.: The Syndrome of Hysteroencephalopathy in Military Psychiatric Casualties, J. Ment. Sc. **91**:104-109 (Jan.) 1945; Shock Therapy in Psychosis: A Possible Rational Basis and Its Clinical Applications Based on Three Years' Experience of Its Use in Military Psychiatry, ibid. **90**:440-553 (April) 1944; Schizophrenia in Military Psychiatric Practice, ibid. **91**:110-112 (Jan.) 1945.

noid schizophrenia with depressive features, catatonic stupors, simple schizophrenia and some types of alcoholic hallucinosis without dementia. Braceland and associates [4] showed that insulin has a delayed action on the blood sugar in cases of schizophrenia, suggesting that an anti-insulin factor may be present in schizophrenia. The effect of insulin therapy on the reestablishment of conditioned reflexes must also be considered. In experiments with rats, Gellhorn [5] and others have shown that previously learned conditioned reflexes subsequently "forgotten," because overcome or blotted out by institution of contradictory or inhibitory conditioned reflexes, were restored in high degree after insulin coma. This suggests that conditioned reflexes which have become inhibited, with resulting psychotic behavior, might be released from inhibition and the psychotic behavior then disappear. Meduna [6] reviewed the biochemical changes occurring during insulin shock and during prolonged narcosis treatment, pointing out that the biochemical changes are similar, and concluded that the clinical improvement is based on the use of any type of treatment which interferes with the enzymatic system of carbohydrate metabolism. Various observations as to whether or not cerebral damage occurs in shock therapy, both insulin shock and convulsive therapy, were reviewed by Lewis,[7] who concluded that in general no permanent organic changes take place in the brain. Although permanent organic changes usually do not occur, a number of patients who failed to respond to insulin therapy and who have remained chronically and severely psychotic have shown improvement after prefrontal lobotomy. A similar therapeutic result may have occurred in patients of a similar type to whom Billig and Sullivan [8] gave protracted insulin shock. Seventy-five per cent of these patients showed definite and prolonged improvement after protracted shocks, and the improvement may have been subsequent to permanent organic changes in the brain.

Recognition of the therapeutic value of insulin subshock therapy is not new. The best description of results is that by Rennie,[9] who found that production of one insulin subshock reaction daily, six days

4. Braceland, F. J.; Meduna, L. J., and Vaichulis, J. A.: Delayed Action of Insulin in Schizophrenia, Am. J. Psychiat. **102**:108-110 (July) 1945.

5. Gellhorn, E.: Further Investigations on the Recoveries of Inhibited Conditioned Reactions, Proc. Soc. Exper. Biol. & Med. **59**:155-161 (June) 1945.

6. Meduna, L. J.: Common Factors in Shock Therapy, Dis. Nerv. System **6**:283-285 (Sept.) 1945.

7. Lewis, N. D. C.: Shock Therapy: Evidences For and Against Damage, Digest of Neurology & Psychiatry, Neuropsychiatric Institute of Hartford Retreat, April 1945.

8. Billig, O., and Sullivan, D. J.: Therapeutic Value of Protracted Insulin Shock, Psychiatric Quart. **16**:1-15 (July) 1942.

9. Rennie, T. A. C.: Use of Insulin as Sedation Therapy, Arch. Neurol. & Psychiat. **50**:697-705 (Dec.) 1943.

a week, resulted in "dramatic relief of anxiety in various kinds of excitement—schizophrenic, manic-depressive, suicidal overactivities and panic states." He further described the effectiveness of the method in averting stupors, quieting excitements, interrupting frightening hallucinations and establishing rapport so that psychotherapy could be utilized. The patients rapidly became relaxed and able to discuss their preoccupations, and their diminishing anxiety was further relieved by ability to talk over much of the highly emotionally charged material that had been bottled up in them. He found that the sedative value of insulin was superior to that obtained from chemical sedatives; not only were the patients quieter and more relaxed during the day, but they were able to sleep at night with little or no chemical sedation. Numerous other investigators and clinicians [10] noted similar results.

One of the reasons that insulin subshock produces such dramatic improvement in cases of psychoses in the Army is that many of the psychoses are not classic schizophrenia (dementia precox), but apparently are "acute schizophrenic reactions," which are less malignant. This conclusion is suggested by the observations of Brill and Walker,[11] who found that without any special treatment almost 50 per cent of a series of 183 patients could be discharged to their own custody or to that of relatives after an average period of hospitalization of about two months. They expressed the belief that the good prognosis of so many of their patients indicated that the psychoses observed in the Army did not carry as grave a prognosis as the similar types developing in civilian life because the military patients had been screened by the examinations of the induction board and the more obviously psychologically unfit already had been weeded out. Their cases came from training camps in this country and occurred relatively early in the war.

10. Appel, K. E.; Farr, C. B., and Marshall, H. K.: Insulin in the Psychoses, Arch. Neurol. & Psychiat. **21**:149-164 (Jan.) 1929. Polatin, P.; Spotnitz, H., and Wiesel, B.: Ambulatory Insulin Treatment of Mental Disorders, New York State J. Med. **40**:843-848 (June 1) 1940. Sargent, W., and Craske, N.: Modified Insulin Therapy in War Neurosis, Lancet **2**:212-214 (Aug. 23) 1941. Sargent, W.: Physical Treatments of Acute Psychiatric States in War, Brit. M. J. **2**:574-576 (Nov. 14) 1942; reprinted, War Med. **4**:577-581 (Dec.) 1943. Tomlinson, P. J., and Ozarin, L. D.: Ambulatory Insulin Therapy: A Report of Fifty-Two Cases, Psychiatric Quart. **16**:167-173 (Jan.) 1942. Gralnick, A.: Psychotherapeutic and Interpersonal Aspects of Insulin Treatment, ibid. **18**:179-196 (April) 1944. Sands, D. E.: Insulin Treatment in Neurosis, J. Ment. Sc. **90**: 767-771 (July) 1944. Moore, M., and Maclean, P. D.: Treatment of Mentally Disturbed Soldiers Overseas, Bull. U. S. Army M. Dept., September 1944, no. 80, pp. 113-118. Minski, L.: War Neuroses, Am. J. Psychiat. **101**:600-605 (March) 1945. Fox, H. M.: Insulin for Rehabilitation, Bull. U. S. Army M. Dept. **4**: 447-452 (Oct.) 1945.

11. Brill, N. Q., and Walker, E. F.: Psychoses in the Army: Follow-Up Study, Bull. U. S. Army M. Dept., August 1944, no. 79, pp. 108-115.

It must be remembered, however, that the patients on whom I am reporting had been psychotic from one to six months before receiving insulin subshock therapy. Because of the duration of psychoses in the cases reported in this paper, the effectiveness of insulin subshock has been very gratifying. It is felt that if these patients had been left untreated, except for general care in the psychiatric ward, many of them would have required eight to twelve months to reach a remission or make satisfactory improvement. Furthermore, the use of insulin subshock reduces to a considerable degree the incidence of tube feeding, mutism, assaults, punitive self injury and frank suicidal attempts and in general quiets or makes cooperatively alert within a few days a patient who on admission was excited, destructive, assaultive or in partial or complete stupor. Another valuable therapeutic result is the rapid, and often amazing, improvement in the physical condition of the patient; at the end of the average four weeks of treatment he has gained from 15 to 40 pounds (6.8 to 19 Kg.), and during the subsequent period of observation he retains on the average about 75 per cent of the considerable gain in weight.

Other psychiatrists in the Army have used insulin subshock therapy for both the psychoses and the neuroses. The results in general have been similar to this author's. Fox [12] used the subshock technic for both the psychoses and the neuroses in a general hospital overseas. He noted in particular a high incidence of improvement and recovery in patients whose psychosis or neurosis had been accompanied with considerable loss of weight. The initial dose of insulin was 30 to 40 units, given once a day, six days a week, and subshock symptoms were allowed to develop to the verge of coma, or until facial twitching suggested that there might be a risk of convulsions. Treatment was given in the morning, and in the afternoon the patient took part in athletics, work details or activities in the crafts shop or went out on pass. Despite the fact that the patients slept most of the morning during the treatment, this did not affect their ability to sleep at night. Treatments were continued from two to four weeks. Fox stated [12]:

> All the psychoneurotic patients were returned to duty and a proportion of the patients with acute psychotic reactions made such good recoveries that after a period of observation on open wards it was possible to return them, also, to full duty status. . . . The treatment has been helpful to a wide variety of patients. It has been used to reinforce the personal psychotherapeutic relationship and to give the soldier enough of a lift so that he can handle his own problems sufficiently well to return to duty.

Fox's experience suggests that this form of insulin therapy, which is relatively easy to give, should be administered as early as possible

12. Fox, H. M.: Insulin Rehabilitation, Bull. U. S. Army M. Dept. **4**:447-452 (Oct.) 1945.

in any acute severe psychotic or psychoneurotic episode, almost regardless of the specific symptoms.

Another Army general hospital in the Zone of the Interior has had an experience similar to Fox's. Missett and associates [13] reported on groups of patients given insulin subshock therapy and/or electroshock therapy. Their technic of insulin treatment was as follows: Treatment was started with a dose of 5 U. S. P. units, which was given three times a day, the amount being increased 5 units per dose until a dose of 40 units was reached. After this, the method was changed to administration of 40 U. S. P. units of insulin intravenously, the patient being left in insulin subshock until he was given breakfast

TABLE 1.—*Results in One Hundred Cases of Insulin Subshock Therapy Reported by Missett and Associates* [13]

	No. of Cases	Complete Recovery, %	Social Recovery, %	Institutional Recovery, %	No Change, %
Cases of insulin subshock	100				
Psychosis, unclassified, with paranoid delusions	50	20	40	20	20
Depressions (manic-depressive, involutional or severe reactive)	11	9	0	0	91
Catatonic schizophrenic reactions	11	0	9	0	91
Hypomanic reactions	?	50		0	50
Schizophrenia or schizophrenic-like psychosis	?	50		50	
Fixed somatic delusions with anxiety	4	100		0	0
Cases of electroshock	33				
Psychosis, unclassified, with paranoid delusions	6	0	0	2	4
Depressions (manic-depressive, involutional or severe reaction) (5 had been given insulin without improvement)	13	60	8	?	?
Catatonic schizophrenia	?	?	40	30	?
Hypomanic reactions	?	?	?	33	?
Schizophrenia or schizophrenic-like psychosis	..	50		50	
Fixed somatic delusions with anxiety	0	..	..		..

at 10 a. m. The intravenous doses of insulin were increased 10 units per day, until a maximum of 100 U. S. P. units was reached. Some patients did not require as much as the 100 unit dose to obtain a satisfactory subshock reaction. The degree of mental confusion accompanying the subshock reaction was measured by certain color charts. Patients continued to receive the intravenous administration of insulin for about six weeks. Table 1 summarizes the authors' results in 100 cases with insulin shock therapy, using the method described. Their results in treatment of psychoses primarily of the paranoid type

13. Missett, J. S.; Perssion, L. B., and Lipton, S. D.: Shock Treatment (Psychotics), in Proceedings of the Neuropsychiatric Conference of the Sixth Service Command, November 1945, pp. 73-77.

were similar to ours; that is, the majority of patients showed improvement or remission. Their results with patients showing primarily a depression differed somewhat from ours; only 9 per cent of their patients given insulin alone recovered, whereas 75 per cent of our patients showed improvement or remission. Of their patients with depression who had failed to respond to insulin and were then given electroshock, 68 per cent showed improvement or recovery. In their comparison of the relative values of insulin subshock and electric shock therapy, they came to the following conclusions:

1. With insulin subshock, the results were satisfactory in treatment of paranoid schizophrenia, psychosis of unclassified type with paranoid ideas, schizophrenia with disorganization and confusion, and hypomania.

2. Insulin subshock was unsatisfactory in the treatment of catatonic schizophrenia and depressed states.

3. Electroshock gave good results in treatment of schizophrenia characterized by confusion and disorganization, excellent results with depressions, fair results with catatonic schizophrenia and poor results in the treatment of hypomania and paranoid states.

4. Insulin seems to be the preferred method of treatment of paranoid states and hypomania. Electroconvulsive therapy is the preferred method of treatment of depressed and catatonic states.

Bloss and Auer [14] used insulin subcoma or subshock therapy in a series of 65 cases of severe anxiety states. The patients had all been evacuated from overseas theaters of war. The technic of therapy, i. e., size of dose, frequency and number of treatments, was not described. A summary of their observations, which is cited in part, presents the following important details:

1. There was evidence of autonomic stabilization, as manifested by decrease in diaphoresis, disappearance of flushing, lowering of elevated blood pressure, slowing of the pulse rate and subsidence of multiple gastrointestinal complaints, including anorexia, nausea and vomiting.

2. Tremors, startle patterns, insomnia, restlessness and other evidences of increased psychomotor activity disappeared.

3. Irritability and aggressiveness disappeared, and the establishment of rapport between the therapeutist and the patient was much facilitated, rendering the concomitant psychotherapy much more effective.

4. The patient entered more readily into the ward activities and the occupational therapy program prescribed for him, and his ability to socialize while in the hospital and on pass progressively improved.

14. Bloss, C. L., and Auer, E. T.: The Use of Subcoma Insulin in the Treatment of Severe Anxiety States, in Proceedings of the Neuropsychiatric Conference of the Sixth Service Command, November 1945, pp. 78-84.

5. There was increased appetite in almost every case. However, the authors were unable to correlate their clinical results with the rate or degree of weight gained, as had previously been described by other authors. Some of the best responses were seen in patients who gained little weight. Although gain in weight of as much as 15 pounds (6.8 Kg.) was observed, the average gain for the series was 4¼ pounds (1.9 Kg.).

The results of treatment are summarized in table 2.

TABLE 2.—*Results of Insulin Subcoma or Subshock Therapy in Sixty-Five Cases Reported by Bloss and Auer*[14]

Diagnosis	No. of Cases	Recovery, %	Much Improvement, %	Improvement, %
Anxiety states	65	34	43	23

TECHNIC OF INSULIN SUBSHOCK THERAPY

A preliminary physical survey is made on all patients who are to receive the treatment. This consists in general physical and neurologic examinations, urinalysis (if possible), blood count, and roentgenologic examination of the chest and electrocardiographic study, or clinical examination of the heart and lungs by the medical consultant if the patient is too disturbed to permit the roentgenogram and electroencephalogram to be taken.

The technic of insulin subshock therapy at this Army general hospital, which is a neuropsychiatric center, is carried out as follows:

Timing of Insulin Injections.—The schedule of injections is as follows:

7 a. m.: Insulin, no breakfast
10 a. m.: Breakfast
1 p. m.: Insulin; no lunch
4 p. m.: Lunch
9 p. m.: Supper

Insulin Dosage.—The first dose varies from 20 to 30 U. S. P. units, depending roughly on the size of the patient's body. Each subsequent dose is increased by 5 units until the desired subshock reaction is obtained. This dose then becomes the "maintenance dose," which later is increased by 5 units as tolerance is developed. As a rule, it takes from three to four days (two injections per day) to reach the reaction dose. The insulin used is regular insulin, preferably in the strength of 80 or 100 U. S. P. units, because this concentration of insulin permits the use of a small volume, and therefore the patient does not get painful lumps at the site of the hypodermic injection.

Ward Setup.—Patients under treatment are kept in a dormitory so that they can be supervised as a single group during the treatment. The arrangement of beds is such that patients ordinarily occupying rooms are moved with their beds to a third row of beds down the center of the dormitory. In this way a sixteen-

bed dormitory accommodates 24 to 30 patients. After the patients receive their injection of insulin, they are free to move around the dormitory or go to the latrine and are kept occupied quietly with group games, occupational therapy, musical programs and letter writing. As they begin to feel weak and start sweating, they usually go and lie on their beds. Very disturbed patients are kept locked in their rooms and visited every fifteen minutes while under treatment for the first few days, until they have quieted sufficiently to join the dormitory group. After an individual treatment period is over, that is, after the meal is given, the patients enter into some group activity, such as a trip to the post exchange soda fountain, to the hospital library or to the gymnasium, depending on whether their behavior at that time permits their leaving the ward in a group. The group leaving the ward usually comprises 12 or 15 patients, supervised by a nurse and two or three ward attendants, who carry with them sugar or candy to be given to any of the patients who happen to show a return of symptoms of insulin reaction. The personnel on duty during the treatment consists of two nurses, three or four enlisted men ward attendants and one or two civilian women attendants. These personnel members are trained to recognize the signs of insulin subshock, and they keep roaming from bed to bed to see that the individual patient does not get too near the coma state. As needed, they help the patient into a sitting position and give him sugared orange juice by means of a spoon or cup, depending on how well he can swallow. The nurse decides when a particular patient shall have his insulin reaction terminated. The ward physician is available nearby for emergencies, but most of the time he is able to work in his office and the treatment program in the dormitory goes on perfectly well without his presence. If a patient has a convulsion, the nurse gives the epinephrine and the intravenous injection of dextrose. If the patient happens to have a second convulsion within a few minutes (and this has occurred very rarely), the ward physician is called and gives further dextrose or stands by while additional treatment is given.

Management of Patient.—Between the time of the first injection of insulin at 7 a. m., and the hour when breakfast is due, and between the second insulin injection, at 1 p. m., and the time when lunch is due, the patient may be given sugared orange juice (50 Gm. of sugar in 250 cc. of orange juice) if the severity of the insulin reaction warrants. The ideal procedure is to produce an insulin reaction bordering on coma, but just before coma occurs the patient is roused by external stimulation, such as calling his name or shaking him, and is given the sugared orange juice, first with a spoon and then by drinking. This amount of carbohydrate makes the somnolence recede sufficiently so that he can eat, and he is given the meal due.

The symptoms of insulin subshock reaction include diaphoresis, which usually is profuse; pallor; weakness; feelings of faintness; unsteadiness; tremulousness; occasional diplopia, and sometimes a change in the patient's usual behavior, so that where formerly restless or excited he becomes quiet and begins to drift into coma, or where formerly retarded and stuporous he becomes excited and overactive.

If it happens that the patient becomes too somnolent to be aroused readily, and therefore cannot take the sugared orange juice by mouth, he is given an intravenous injection of dextrose (25 to 50 cc. of 25 per cent dextrose), which then is followed with sugared orange juice and then the meal due. We do not bother with tube feeding, because it is seldom that the patient slips into coma, and an intravenous injection of dextrose solution can be given much more conveniently and with no risk to the patient.

COMPLICATIONS

The chief complications to be considered are irreversible coma, acute pulmonary edema or atelectasis, and convulsions, which may be complicated further by fracture of the vertebrae. We had 1 fatality from irreversible insulin shock. This occurred in a 22 year old soldier in excellent physical condition, who had been acutely psychotic for about three months. On the fifth day of treatment, during which he had not shown as yet any insulin subshock reaction, he suddenly went into full shock, about twenty minutes after the 1 p. m. dose, which was 60 units. It is of significance that he had had sodium amytal, 3 grains (0.195 Gm.), by mouth the preceding night at 11 p. m. and again at about 5 a. m. We knew from experience that barbiturates were somewhat dangerous in that they make the patient more sensitive to insulin reactions. Even though sodium amytal may have been a factor in the unexpected and sudden development of full coma, there was probably an associated allergic response of an unknown type. The patient was given hypertonic solution of dextrose, 5 per cent dextrose in saline solution, oxygen and other restorative measures, but symptoms of decerebrate rigidity developed and then terminal pneumonia. He died three days later, without regaining consciousness.

The outline of treatment of protracted insulin shock is as follows:

1. Intravenous administration of a 25 per cent solution of dextrose, at least 150 to 200 cc., repeated hourly until the blood sugar is well over 200 mg. per hundred cubic centimeters and/or specimens of urine show a 4 plus reaction for sugar. 2. Administration of oxygen or "carbogen" (95 per cent oxygen and 5 per cent carbon dioxide) by mask whenever there is any evidence of respiratory difficulty or cyanosis. If the need for oxygen is prolonged, the patient should be placed in an oxygen tent.

3. Injection of vitamin B complex, thiamine hydrochloride and niacin (nicotinic acid) in large doses parenterally.

4. Transfusion of whole blood, at least 500 cc., if the patient has not reacted satisfactorily within four hours after the onset of coma.

5. Administration of hypertonic saline solution, 1,000 cc., by venoclysis if the patient shows increasing fever (it offsets loss of chlorides from sweating and helps to combat cerebral edema).

6. Spinal drainage. The initial pressure should be recorded carefully and the pressure then reduced to 150 mm. water by slow drainage. This should be done if the patient has not reacted satisfactorily within eight hours of the onset of coma and should be repeated every eight hours as long as coma is present.

Occasionally a patient, after having symptoms of subshock reaction for about an hour, rather suddenly became dyspneic and cyanotic. Inhalation of oxygen by means of an oronasal mask for a few minutes, together with intravenous injection of a hypertonic solution of dextrose, resulted in disappearance of these symptoms of respiratory distress.

None of these patients had any significant pulmonary edema, which is relatively common in cases of insulin full shock and sometimes is extremely difficult to manage.[15] Three patients had a mild degree of atelectasis secondary to inhalation of orange juice but experienced no special difficulty, and treatment was continued as usual. Occasionally a patient would show a return of subshock symptoms about noon or 7 p. m.; sugared orange juice was given by mouth to relieve the symptoms and the next dose of insulin administered given as usual.

Convulsions require special attention. In about 10 per cent of the patients generalized convulsions occurred once during the four week period of treatment. There was only 1 occurrence of vertebral fracture; in this instance there developed a moderate degree of typical compression fracture of the third and fourth thoracic vertebrae. If the patient showed much facial or generalized muscular twitching, suggesting an impending convulsion, he was given sugared orange juice by mouth. If a patient had a convulsion, he was given 0.3 cc. of a 1:1,000 solution of epinephrine hydrochloride hypodermically. This mobilizes the glycogen in the liver, causing the patient to relax and delaying any impending convulsion sufficiently long to permit the patient's being given dextrose intravenously (25 to 50 cc. of a 25 per cent solution). After the intravenous administration of dextrose, he is given sugared orange juice by mouth and then the meal due. When a convulsion has occurred, the next dose of insulin is given at the usual time, but the dose is cut one third, and subsequent doses are increased 10 units per dose until a satisfactory subshock reaction dose is reached again. It has been suggested that diphenylhydantoin sodium might be given routinely in a dose of 0.1 Gm. daily while the patient is receiving insulin subshock therapy so as to decrease the possibility of convulsions. This medication was not given in the cases reported in this paper.

Significant complications and their incidences are shown in table 3.

Occasionally, in the case of a severely excited patient in whom we want to obtain the sedative effect of insulin as quickly as possible, we give an additional dose of insulin at 7 p. m., followed by supper at 10 p. m. and a fourth dose of insulin (in twenty-four hours) at 1 a. m. and a meal at 4 a. m.; then the usual insulin schedule is resumed.

Insulin subshock treatment, therefore, is given twice a day, seven days a week, as previously described, except on rare occasions, on which a particular patient may be given three or four doses in twenty-four hours until his excited condition is controlled; then he goes on the

15. Gottesfeld, B. H.; Qintana, P. A., and Fourzan, E. D.: Further Studies in Pulmonary Edema Associated with Insulin Shock Therapy, Digest of Neurology and Psychiatry, Neuropsychiatric Institute of Hartford Retreat, Sept. 1945, pp. 689-694.

regular schedule of two doses per day. The patient is kept on insulin subshock treatment for a sufficient period to give him approximately three weeks of satisfactory subshock reactions. This means that the whole treatment takes about four weeks, because a preliminary three to five days is needed to work the patient up to satisfactory subshock reactions and from three to five days to taper off. The tapering-off process is more rapid than the building up; the dose is reduced 15 units at a time.

THERAPEUTIC RESULTS

The majority of patients treated had a diagnosis of "psychosis, unclassified, acute schizophrenic reaction," and in most of these patients the disease showed considerable improvement or was in remission. Many of these patients had been psychotic three or four months before reaching this hospital from overseas; despite such a long duration of

TABLE 3.—*Complications of Insulin Subshock Therapy and Their Incidence in a Series of 393 Patients Treated with the Insulin Subshock Method*

Complication	Total No.	No. of Patients Treated	Incidence, %	Comment
Irreversible coma, fatal termination	1	393	0.25	Occurred on fifth day of treatment with dose of 60 units
Convulsion	40	393	9.9	10% of patients have one convulsion some time during the thirty days of treatment
Fracture of vertebra during convulsion	1	393	0.25	

symptoms, the majority still responded well. The patients who failed to improve were those with hebephrenic schizophrenia, manic states and atypical depressive states with elements of schizophrenia. All our patients whom the insulin therapy failed to benefit received a course of electroshock treatment (twelve convulsions, given at the rate of three per week). The patients with manic states responded fairly well to electroshock; they were given insulin as the first type of specific treatment, for sedative and nutritional reasons. This therapeutic method of giving first insulin subshock and then electroshock was also carried out with the patients with depressive states for the same (nutritional) reason. Experience in civilian life had indicated that the most effectual way of using the two treatments was to give insulin subshock first, following with electroshock as needed. If the procedure is reversed, and electroshock is given first, the patients who show symptoms of depression and schizophrenia usually lose the symptoms of depression but the schizophrenic symptoms are not modified. Since the schizophrenic symptoms are considered more malignant, it is felt that they

should be relieved as soon as possible and then any remaining significant degree of depression may be treated with electroshock. Other workers disagree with this opinion.[16] Data on the total number of patients treated, including both psychotic and psychoneurotic patients, are presented in table 4.

SUMMARY

It has been found that insulin in subshock doses is of considerable therapeutic value in treatment of the dementia-precox–like psychoses (diagnostically called "psychosis, unclassified, acute schizophrenic reaction") and the undiagnosed psychoses which have schizophrenic features. After the first few subshock reactions there is a marked reduction in, and finally disappearance of, such symptoms as confusion, negativism, feelings of unreality, catatonic excitement and catatonic stupor. There was no satisfactory permanent therapeutic result in cases of severe, prolonged schizophrenia and in about 50 per cent of cases of hypomania. Insulin subshock produced considerable improvement in the patients' physical condition, particularly those who were poorly nourished, and this made any necessary electroshock treatment less hazardous.

Early in this series, we tended to transfer patients to a veterans' hospital before they had sufficient insulin subshock, and follow-up statistics on these patients show that our early policy was not correct. Even before this follow-up information was obtained, we had changed our policy to that of giving what we felt was sufficient insulin subshock, followed by an adequate period of observation before arranging transfer to the veterans' administration facility. Since that plan was instituted, we have been able to reduce the proportion of patients being sent to veterans' hospitals. For the past six months only 10 per cent of patients, who were psychotic on admission, have had to go to the veterans' hospitals.

Our primary aim has been to give our psychotic patients insulin subshock therapy practically regardless of the clinical diagnosis, because we have seen unexpected improvement and remissions in patients who ordinarily would have been considered destined for many months, or perhaps indefinite years, of hospitalization. What the subsequent outlook is for relapse in these patients who have improved rapidly under insulin therapy with or without supplemental electroshock remains to be seen. Subsequent follow-up studies will be made to see whether these patients relapse soon after return to civilian life and have to be rehospitalized. We still feel that as much intensive treatment should be given as early as possible, in the hope of preventing psychotic patients

16. Weil, A. A., and Moriarity, J. D.: Insulin Therapy in Schizophrenia Patients Responding Unsatisfactorily to Electroshock Treatment, Dis. Nerv. System **5**:334-337 (Nov.) 1944.

from continuing in or progressing to a chronic psychotic state requiring indefinitely prolonged care in the hospital.

Our results in using intensive insulin subshock therapy with the patients with severe psychoneuroses of the anxiety–tension state type have been very satisfactory. Since this hospital is a general one in the Zone of the Interior, the psychoneurotic patients admitted from overseas all had severe, long-standing disorders. A review of their overseas medical records showed the frequent use of such specialized treatment

TABLE 4.—*Data on the Entire Series of Patients*

Mental Disorder	Number and Percentage of Cases	Average Age, Yr.	Average Time in Service	Service		
				Not Overseas	Overseas	Unknown
oses						
Total number	324	26	2 yr. 4 mo.	82	233	9
Percentage	100	.	.....	25.3	71.3	2.7
ophrenia						
Total number	118	27	2 yr. 5 mo.	36	80	2
Percentage	100		.....	30.5	67.8	1.7
atatonic	27	23	2 yr. 3 mo.	5	22	0
ebephrenic	8	25	2 yr. 8 mo.	1	7	0
aranoid	45	28	2 yr. 6 mo.	15	29	1
imple	18	25	2 yr. 5 mo.	8	9	1
ixed	4	25	1 yr. 4 mo.	1	3	0
nqualified	16	29	3 yr. 3 mo.	6	10	0
-depressive psychosis—total number	7	29	2 yr. 3 mo.	1	6	0
ypomanic	6	28	2 yr. 5 mo.	1	5	0
epressed	1	34	1 yr. 6 mo.	0	1	0
oses, unclassified						
Total number	178	26	2 yr. 4 mo.	36	140	2
Percentage	100	.	.....	20.2	78.7	1.1
cute schizophrenic reaction	141	25	2 yr. 4 mo.	22	119	0
ypomanic reaction	8	26	2 yr. 2 mo.	1	7	0
epressive reaction	5	30	2 yr. 3 mo.	0	4	1
aranoid reaction	12	28	2 yr. 7 mo.	7	4	1
nqualified	4	27	1 yr. 7 mo.	3	1	0
ixed	8	25	2 yr. 4 mo.	3	5	0
ic psychoses (post traumatic)	2	23	2 yr. 6 mo.	0	2	0
oses with mental deficiency	8	26	2 yr. 3 mo.	4	3	1
oses with psychopathic personality	9	25	1 yr. 7 mo.	5	2	2
llaneous forms	2	28	3 mo.	0	0	2
oneuroses						
Total number	69	27	2 yr. 3 mo.	31	33	5
Percentage	100	..	.....	44.9	47.8	7.3
ysteria	8	22	1 yr. 6 mo.	4	4	0
nxiety state	17	30	2 yr. 2 mo.	8	7	2
eactive depression	12	27	2 yr. 6 mo.	5	6	1
ypochondriasis	2	30	2 yr. 11 mo.	0	2	0
bsessive-compulsive neurosis (psychas-thenia)	1	33	2 yr. 9 mo.	0	1	0
ixed type	29	28	2 yr. 3 mo.	14	13	2

methods as those of pentothal or sodium amytal abreaction and narcosynthesis, continuous narcosis for three to ten days, insulin subshock and insulin full shock. We were particularly interested in how the insulin had been given, and we noted that if full shock was used the treatment was given over a very short period, usually daily for five or ten days. When insulin subshock was used, we noted, again, that the duration of treatments was too short and the dose almost invariably too low (the average maximum was 80 units) and given only once a day, six days a week for a week or two. Our results with sodium amytal nar-

cosynthesis or with "modified insulin subshock" (a maximum dose of 50 units twice a day) were discouraging, but when we gave the patients intensive insulin subshock, with the technic outlined in this paper, the results were excellent. The psychoneurotic patients selected primarily for intensive insulin subshock were those with the severe anxiety-tension states, manifested by tremulousness, startle reaction, battle dreams and often such other symptoms as hyperhidrosis, neurodermatitis, dilated pupils, emotional instability, depression and episodes of

Treated with Insulin Subshock Method

Shock Therapy		Condition on Leaving Hospital				Type of Disposition			
Insulin Subshock	Insulin plus Electric Shock	Unimproved	Improved	In Remission	Recovered	Veterans' Hospital	Discharged to Custody of Self	Discharged to Duty	Other Disposit
324	102	58	82	167	16	83	228	0	13
100.0	31.5	17.9	25.3	51.6	5.0	25.6	70.4	0	4.0
118	62	41	44	30	3	61	54	0	3
100.0	52.6	34.8	37.3	25.4	2.3	51.7	45.8	0	2.5
27	16	10	6	8	3	13	13	0	1
8	3	5	2	1	0	7	1	0	0
45	30	19	17	9	0	27	18	0	0
18	2	0	10	8	0	5	13	0	0
4	1	1	2	1	0	1	3	0	0
16	10	6	7	3	0	8	6	0	0
7	3	1	2	3	1	1	6	0	0
6	3	1	1	3	1	1	5	0	0
1	0	0	1	0	0	0	1	0	0
178	36	9	30	130	8	10	152	0	7
100.0	20.2	5.0	17.0	73.0	5.0	10.7	85.4	0	4.0
141	32	3	16	115	7	11	126	0	4
8	0	0	4	3	0	0	7	0	1
5	0	2	1	1	1	2	3	0	0
12	2	3	4	5	0	4	8	0	0
4	0	1	3	0	0	2	0	0	2
8	2	0	2	6	0	0	8	0	0
2	0	0	0	0	2	0	2	0	0
8	1	2	4	2	0	1	6	0	1
9	0	5	2	2	0	1	8	0	0
2	0	0	0	0	2	0	0	0	2
67	0	4	61	1	3	0	62	3	4
100.0	0	5.8	88.4	1.5	4.3	0	90.0	4.4	5.6
8	0	0	6	1	1	0	8	0	0
17	0	1	15	0	1	0	14	1	2
12	0	0	11	0	1	0	10	1	1
2	0	0	2	0	0	0	2	0	0
1	0	0	1	0	0	0	1	0	0
29	0	3	26	0	0	0	27	1	1

acute panic reactions. Given a patient of this type, one would see the symptoms begin to disappear on the fifth or sixth day of satisfactory insulin subshock reactions. The patient would gain weight rapidly and become relaxed, cheerful and extremely cooperative. No other method of treatment that we have tried will produce such amelioration of symptoms so rapidly. How long this improvement will be sustained we are unable to say, but the rapidity with which the symptoms of severe tension states melted away was impressive. The only psychotherapy employed was based on using the patient's symptomatic improve-

ment to impress on him that his prognosis was excellent and he soon would be well again. The results were so striking that we began using insulin subshock therapy with any type of severe psychoneurosis when the patient either showed no improvement after two or three weeks in the hospital or had a severe reactive depression, requiring care in the closed ward because of risk of suicide, at the time of admission.

ILLUSTRATIVE CASE HISTORIES

CASE 1.—A private first class, unassigned, aged 27, with two years and eleven months of service, was admitted on Sept. 6, 1944, with a diagnosis of dementia precox, hebephrenic type.

TABLE 5.—*Data on Patients Treated with Insulin Subshock from April 1, 1944 to Nov. 30, 1945* *

	Number	Per Cent
Patients treated	324	
Discharged to self	228	70.37
Transferred to Veterans' hospitals	83	25.62
Transferred to other Army hospitals	13	4.01

During the last six months of this period 90 per cent were discharged to self and only 10 per cent to Veterans' hospitals.

TABLE 6.—*Follow-Up Observations on First Twenty-Five Patients in Veterans' Hospitals*

Condition	Discharged Recovered	Discharged Improved	Discharged Unimproved	Still in Hospital
According to records of Veterans' Administration Facility	3	12	6	4
Average days in Veterans' hospitals	17	41	110	148

Relevant History.—The patient had been brought up in a rather strict home and was dependent on his mother, to whom he had formed a strong attachment. He had a twin brother, who was of an opposite type of personality. His maternal grandfather committed suicide because of "nervous strain." The patient's early history was without significance except for temper tantrums, terrifying dreams and talking in his sleep. The patient had completed four and a half years of college but did not receive a degree and had never had a steady job, working mostly with his father in their laundry. He gave the usual story of masturbation but had socialized little with girls, not having had a date since being in the Army.

Present Illness.—The patient was hospitalized overseas on July 18, 1944, after being in Hawaii over two years. He had grown nervous and tremulous, began to feel that groups of soldiers were talking about him, seemed preoccupied and was seen to laugh without motivation. Prior to that date he had been a poor mixer but had performed adequately.

Physical Examination.—Physical and laboratory examinations revealed nothing abnormal.

Mental Status.—The patient was manneristic, with grimacing and unmotivated laughter, moderate psychomotor overactivity and much gesticulating. His manner was effeminate; speech was careful and somewhat stilted, and his productions were mildly disconnected. His mood had been variable, being frequently euphoric and at times showing dissociated affect and silly laughter. No other delusions or hallucinations could be elicited. The sensorium was clear, the judgment superficial and insight partial.

Course in Hospital.—The patient was placed under insulin subshock routine therapy. He received insulin for twenty-three days, the maximum dose being 145 units and the total stay in the hospital fifty-one days.

Final Diagnosis.—The diagnosis was psychosis, unclassified, acute schizophrenic episode.

Condition.—The disease was in remission at the time of the patient's discharge.

Disposition.—He was discharged to his parents' custody.

Comment.—The patient originally had a definite schizoid personality and had shown severe schizophrenic symptoms for two months before receiving insulin; yet the psychotic symptoms cleared rapidly.

CASE 2.—A private aged 33, with one year and nine months of service, was admitted Nov. 18, 1944, with the diagnosis of dementia precox, simple type.

Relevant History.—The patient's family lived in Denmark. The father was emotional and domineering; the mother, who had been diabetic, died of cerebral hemorrhage while the patient was in the service. The patient was the oldest of 3 siblings; he had had enuresis until the age of 14, with recurrent terrifying dreams of being taken away from his father "by the moon." He had been a frail child and had suffered from chronic bronchitis and associated fevers. During fevers he would dream of coasting down a slide on rough sandpaper; he gritted his teeth in sleep. There was rivalry between the patient and his youngest brother, who was idolized because he was so much younger. The patient graduated from high school and attended one year of business college, majoring in languages and architectural drafting; he attended school only because he had to. He began working in a ship broker's office; at the age of 19 he came to America for a visit and stayed. He attended high school here to adjust more adequately. He held many odd jobs until he had worked himself up from common laborer to an electrical draftsman for a utility company. He had been happily married for ten years, though disappointed because of his wife's sterility. He planned to adopt a child after service. The patient seldom became angry, but then flew into a rage. Ordinarily, he was shy, reserved and somewhat overattentive to his health; he was impatient, had an "active conscience" and had to know why a thing is done.

Present Illness.—He was first hospitalized at a station hospital in California, having been transferred from the guard house on Nov. 15, 1944, after an incident in which he tried to board a truck going to the flight line and was forcibly ejected. He said he thought he was going to the gate and was rather excited at the time. He stated that he had been well and normal until two months previous to hospitalization, when he was a casual in Georgia. He began to notice that he was restless, uneasy and nervous. This state increased in intensity and was followed by tremulousness, forgetfulness and inability to concentrate, insomnia, nausea and vomiting after meals and loss of appetite.

Physical Examination.—The patient was thin, undernourished and dehydrated, but his condition was otherwise normal.

Laboratory Examination.—Laboratory studies revealed nothing abnormal.

Mental Status.—The patient was transferred here three days after the incident on the truck and was admitted to the prison ward; he was then transferred to a closed ward because he was psychotic. He was greatly underweight, unkempt and disheveled and extremely confused and bewildered. He had great difficulty in thinking and expressing himself; speech was meager but coherent. He seemed anxious to talk but was unable to do so; he described a feeling of being controlled not only by people but by nature; he was actively hallucinated in the auditory sphere and extremely tense and anxious regarding what would happen to him, and he resented being placed in a closed ward. At times he was practically mute. He was unable to go near his bed, but stayed around the outer door with a hunted, frightened expression. He often seemed confused and wandered about aimlessly. An explanation of insulin treatment was given, and an effort made to secure his confidence was partially successful.

Course in Hospital.—The maximum dose of insulin administered was 125 units, the period of insulin therapy twenty-two days and the period of hospitalization seventy-one days. The patient's appetite improved almost immediately after initiation of insulin therapy, and the first subshock reaction occurred with a dose of 125 units. While in the subshock state, the patient became affectionate, euphoric and aggressive in his advances toward members of the personnel, in contrast to his usual anxiety, depression and seclusiveness. His anxiety began to disappear after the third subshock reaction, and cooperativeness and initiative progressively improved until the course of treatment was finished. He gained weight and self confidence, became pleasant and cooperative and was a model patient; all ideas of reference, delusions or hallucinations had disappeared with the development of insight.

Final Diagnosis.—The diagnosis was "psychosis, unclassified, acute schizophrenic reaction."

Condition.—The disease was in remission at the time of the patient's discharge.

Disposition.—He was discharged to his own custody with a certificate of disability.

Comment.—On his admission the patient's condition resembled the catatonic type of dementia precox rather than the simple type. The response to treatment was rapid.

CASE 3.—A private of the ordnance division, aged 19, with two years of service, was admitted on Aug. 11, 1944, with the diagnosis of psychosis, unclassified.

Relevant History.—The patient was the third of 3 siblings; there was no history of abnormal development; he attained the eleventh grade at the age of 16 and apparently socialized well. His record revealed nothing of significance. Psychosexual development was apparently normal. Although the patient had no actual conflict with the law, he apparently associated with gangs engaged in petty thievery but was never apprehended. He had had little supervision in his early home life; he had usual interests in amusement found in his cultural group, but had received little religious training. He stated that at one time he drank excessively. He denied having had venereal disease.

Present Illness.—On April 17, 1944, while in New Guinea, the patient sustained a head injury and was unconscious "about fifteen seconds." This required no hospitalization, but he stated that his illness started at that time. He was injured in a jeep wreck on May 1, 1944; this required hospital care, but he recovered

and returned to duty. About June 24 he began to show mental symptoms, becoming incoherent, rambling, silly, hallucinated and overactive; he expressed ideas of reference and grandeur and required care in a closed ward.

Physical Examination.—The blood pressure was 110 systolic and 64 diastolic. The heart and lungs were normal. The general physical condition was good.

Laboratory Examinations.—The results of laboratory tests were normal.

Mental Status.—The patient was restless, overactive, euphoric and often rather silly. On his admission no hallucinations or delusions could be elicited, although previous records described both auditory and visual hallucinations, confusion, disorientation and impairment of intellectual faculties in general

Course in Hospital.—The patient was placed under routine insulin subshock therapy for thirty days, the maximum dose being 185 units and his total stay in the hospital one hundred and twenty-five days.

Final Diagnosis.—The diagnosis was psychosis, unclassified, manifested by a manic episode with schizoid features.

Condition.—The disease was in remission.

Disposition.—The patient was discharged to his own custody.

Comment.—This case is similar to case 4, in which a manic-schizoid mixture gave an excellent response to insulin subshock therapy. The patient was well enough for discharge a month before he was actually released, but in the pressure of work he was overlooked.

CASE 4.—A corporal, unassigned, aged 33, with two years and four months of service, was admitted on June 23, 1944, with a diagnosis of dementia precox, paranoid type.

Relevant History.—The patient had been an only child in a harmonious home; his father was a minister, who died when the patient was 12; the boy was subsequently raised in an orphanage. He exhibited no neurotic traits in childhood. He was not a good student because of day dreaming, but he liked selling, competition and sports. He had been an extroverted, mildly hypomanic type all his life and had many friends in the theater and business worlds. A former marriage to an older woman had been unsuccessful. He had been divorced, and for the past year had been enthusiastically engaged to a girl somewhat younger than himself.

Present Illness.—The patient was hospitalized overseas, on April 2, 1944, because he had been making prophecies to men in his outfit, writing letters to world figures on the conduct of the war and styling himself as Jesus Christ and a "five star general." He stated that he had had a revelation on March 19 and that he was empowered to predict the end of the war. At that time he exhibited bizarre and silly behavior, hallucinations and delusions and dissociation of mood and thought, and was untidy. A diagnosis of dementia precox, hebephrenic type, was made, and he was evacuated to the mainland. On admission he was extremely euphoric, delusional and disoriented.

Physical Examination.—His condition was essentially normal except for a blood pressure of 185 systolic and 85 diastolic, which rapidly decreased as his excitement subsided.

Laboratory Examination.—Laboratory tests revealed nothing abnormal.

Mental Status.—He was disoriented, but not grossly confused, and exhibited psychomotor hyperactivity; he expressed delusions of grandeur, stating that he

was Christ and "a five star general." He talked and laughed constantly, promoted every one who pleased him and "busted" those who did not. The condition appeared primarily to be a schizoid-manic psychosis with expansive delusions.

Course in Hospital.—He received the routine insulin subshock treatment for twenty-four days, the maximum dose being 25 units and the total stay in the hospital ninety-two days.

Final Diagnosis.—The diagnosis was psychosis, unclassified, manifested by manic behavior, delusions of grandeur, disorientation, religious preoccupation, flight of ideas, verbigeration, preliminary depression with suicidal ideas and regressive behavior.

Condition.—The disease was in remission.

Disposition.—The patient was discharged to his own custody.

Comment.—The diagnosis is better formulated as psychosis, unclassified, manic reaction with schizoid trend. The records indicate that there was considerably more schizophrenic coloration overseas than when the patient arrived here. Despite the acutely severe psychotic symptoms for three months before insulin subshock therapy, a remission occurred after only fifteen "reactions." When the acute symptoms disappeared, he remained perhaps slightly hypomanic, although his friends said that that was his normal "salesman personality." On admission he had been considered suitable for electric shock, but failure in equipment interfered; so insulin therapy was started and produced rapidly an unexpected degree of improvement. An autobiographic account of his psychotic experience follows.

"I WAS AN INSULIN PATIENT"

"The mounting toll of mental cases in this war is obviously increasing by the hour. Few people realize what the individual soldier goes through, when 'out of a clear blue sky' his mind goes to pieces and he cracks up, not only mentally but physically as well. Thus he becomes absolutely useless to the Army and to himself. He not only becomes unfit for service overseas, but if not taken into immediate custody by medical authorities is very apt to be the cause of many of his buddies losing their lives on the battlefield unnecessarily.

"For eighteen months in a midwestern Army post, I put my heart and soul into the war effort, helping religiously to train other men for overseas duty, until finally the time came (and with those orders a terrific lump rises in every man's throat) for me to join a regular outfit destined to work and fight, if circumstances warranted it, on an island in the Pacific.

"The law of self preservation is invariably first and uppermost in a man's mind. Yet, with our nation at war, there is a feeling of 'duty-to-preserve-the-life-of-others-at-home'; if the call comes through, of 'kill or be killed'; and 'Give the enemy hell, son, we've got to win,' is voiced by the company commander.

"At our port of embarkation (P.O.E.) the finishing touches were applied to personal body and equipment. A check and double check was made by officials to ascertain that nothing of importance was overlooked, regardless how trivial and insignificant the detail might seem. Far away from the continental limits of the United States of America, a unit or command has little or no opportunity to make requisition of articles that were missed on leaving the shores of our beloved homeland.

"A tension arose among men awaiting shipment at the P.O.E. that is difficult to describe, especially when our group were put on the 'alert,' which meant, of course, that no mail would go out, no telephone calls could be made and no visitors allowed. Every one was confined strictly to their barracks, with nothing to do except play cards, tell exaggerated stories and speculate as to where they were going, the time of departure and so forth.

"In all my military career, I never heard rumors spread so thick and so fast as at that particular time. They were merely words and conversation; yet they instilled stark f-e-a-r into the minds of many men. Aboard the transport and sailing out of port, these fears persisted throughout the day and half the night. To accentuate them aboard ship were the evening black-out, the zigzag course of the convoy and the precautions the Navy takes against a surprise attack at sea.

"Life while traveling on an Army transport consists mostly of gripes; complaints and constant grumbling; 'bull sessions' in convenient corners of the deck; basking in the sun; eating chow standing up in a crowded and unventilated mess hall, where the food was swished from one end of the table to the other, and loss of appetite on entrance, seasickness and sleep. Shaving and washing the hands and feet were ordeals that one purposely 'put off' until some superior officer came along and threatened a court-martial unless his request was complied with immediately.

"'I hate war! Eleanor hates war!' was a frequent remark overheard daily above and below decks. Also, 'They can't do this to me—I have my rights. Why doesn't this tub go faster, so we can get this damn war over with and go home?' Wherever a gathering of men stood talking, there was bound to be a G.I. who would butt in and say, 'Shall we discuss women now, or shall we lead up to the subject little by little?' If the women at home only knew how much they are talked about by their fighting he-men overseas—and if they only knew how much they are missed, hated, cussed and loved by those fighting sons of freedom.

"After days of monotonous travel, roll-called, pushed and crammed into trains, trucks and buses, we arrived at our destination. Work assignments began at once. From that moment on, it was all work and no play seven days a week. The only relaxation several of the boys in my outfit found was drinking bay rum and 'Aqua Velva' shaving lotion mixed with lemon extract and Cocoa-Cola during the couple of hours each evening they were off duty. Of course, the following day they were 'fit to be tied.'

"When I left the States, I had a 'hope' in my mind and heart that the war would be over, completely over, by June 30, 1944. As the weeks and months went by, that fact became an obsession with me. The more physical strength I exerted in my daily tasks, the more positive my mind became that the war would end on June 30. I talked about it, dreamed about it, wrote about it to friends back home and was quite successful in making the majority of men in my outfit believe that the war would end, not only on June 30 but that at exactly 10 a. m. on that Friday morning a document would be signed on the U. S. cruiser *Augusta* 5 miles off the British coast and the signature would be, first, Franklin Delano Roosevelt; second, Winston Churchill; third, Joseph Stalin, and, fourth, Adolph Hitler, who would then be a political prisoner of war in the hands of the Allies. Japan, I maintained, would collapse like an accordion and fall helpless to the Allied nations on June 25. I claimed the 10 a. m. to be Greenwich time, English time, or the time of Winston Churchill's wrist or pocket watch, whichever he might be wearing on that famous day.

"On pay day, March 31, the beginning of my total 'crack-up' came. On receiving my pay envelope, I tore it open and proceeded seriously to give away money to my buddies. The mental illusion I had was this—I needed no money because, having written the prophecy affixed with twenty-one signatures as witnesses, when the war ended, as prophesied, I would then become an extremely wealthy man. When asked what would I do 'if' the war didn't end at that time, I replied, 'It's utterly impossible for it *not* to end at exactly 10 a. m., June 30, and not one minute before, or one minute after.' That's how positive I was in that frame of mind.

"Not over a quarter of a mile from our hillside detachment was a small community church. On Sunday morning during the services I sauntered nonchalantly in while every one had their heads bowed in prayer and walked with head erect to the front platform where the minister was solemnly speaking and sat down in his chair behind the pulpit. When he finished, I got up on my feet and addressed the congregation in a loud and domineering voice, exclaiming that I was the one and only true prophet who had come at last to relieve the world of its suffering and end the war with divine guidance and divine power, which had been bestowed on me by God himself.

"At that juncture, two young military men left their seats and stepped up on the platform, and with dignity and grace politely escorted me to the exit, where they told me I better return to my detachment. Word quickly reached my acting first sergeant about my unusual and startling behavior, and that same afternoon I was taken before an Army medical officer, who gave me a thorough examination and then ordered me confined behind closed and barred walls in a ward at the nearest overseas station hospital.

"As the key turned in the lock behind me, I suddenly believed that I was being protected by our government from enemy eyes and ears and would be safeguarded as such until June 30 arrived. However, one thought puzzled me tremendously. I couldn't seem to understand the attitude and remarks of the other patients around me. To me, I was the only one who acted and talked sensibly. It made me quite happy to have the doctors, nurses and ward boys agree to everything I said and did. I was somewhat abashed, though, when I was unable to reach the President of the United States of America by long distance telephone. I had so many wonderful suggestions and ideas to convey to him personally, ideas that I knew would help him conduct the war to a successful conclusion and prepare America and the world for a thousand years of peace in his postwar setup.

"The daily routine which followed my incarceration in ward 14 consisted of eating, drinking fruit juices, bathing, and talking and talking and talking—well, in fact, I decided that circumstances had placed me as the star performer within the scope of television, and that pictures and sound effects were recording everything I did and every word I spoke; therefore I talked constantly without pause or break for twenty-two hours out of twenty-four. When others went to sleep at night, I cut my tone down to an audible whisper. Pills filled with sedative powders put me to sleep for the remaining two hours.

"To make my performance more outstanding before my unseen audience, which I tried hard to compel ward boys and fellow patients to understand was present, although they could not see the cameras and interested spectators, I wrote daring letters to the Pope of Rome, Adolph Hitler, General MacArthur, Cordell Hull and other world-renowned personalities. And, of course, to top that off, I wrote signs and symbols, parables and what have you, in books, magazines and on the walls of the hospital ward. My sincerity knew no limit. When-

ever a question was put to me by a doctor, nurse or ward boy, a question pertaining to current events, my former military status or my past life, I could always answer truthfully and in an apparent sane and logical manner. But as soon as the questioning was over, I invariably swung back into my role as the one and only true prophet who had come to straighten out world affairs. My mind was focused on June 30, for every day I was more positive than ever that on that date all mystery as to who I really was would be quickly cleared up and world popularity would be mine.

"In the latter part of April I was transferred to another overseas hospital, located on an island some distance by water from the one where I had left my buddies and outfit. At a board meeting of medical men prior to my departure, I was voted 'unfit for overseas service' and recommended for hospitalization back in the States.

At general hospital X in the mid-Pacific, much to my surprise and consternation, I saw hundreds of men with mental disorders all destined for home as soon as transportation could be arranged. All were confined in closed and barred wards, with high fences surrounding the grounds. The policy of that hospital was strict and rigid. All personal items were taken from the men. No matches to go with cigarets. No entering a lavatory without a ward boy. No toilet articles, especially razor blades, were permitted out from under lock and key unless an attendant was present. To smoke a cigaret one had to ask the ward boy for a light. Temperatures were taken twice daily by nurses. Sleeping sedatives were issued nightly. To prevent men from committing suicide, straitjackets had to be used occasionally. In ward 27, where I was confined, anything was likely to happen at any moment. Doctors, nurses and ward boys were always on guard, never letting a single patient out of their sight for a moment. It must be remembered, all patients were victims of a cruel, tortuous war against an enemy that is ruthless and vicious in every conceivable way.

"The diagnosis in my case was a total nervous breakdown, mentally and physically; but of the men I met at general hospital X, over 60 per cent were shell shock cases, and what pitiful sights they were. At that particular hospital treatments were difficult to administer, owing to crowded facilities and the desire to get men back to the States as soon as possible. Severest of all cases are those in which the men also have malaria, and fever overcomes them when least expected. Individual locked rooms contained the patients whom it was thought by authorities might 'blow their top any moment.' . . . These men would yell and scream and cry with tears flowing from their eyes and bang themselves against the walls of their room. Many refused to keep their pajamas on and nakedly pranced around their room like wild animals in a cage at the zoo. All furniture except a rubber-covered mattress had to be eliminated, so that the patient wouldn't hurt himself.

"At this point I wish to analyze the term 'shell shock,' which is familiar in connection with the first world war. If any person is going about his business in daily life and suddenly, without premonition, an explosion is heard close to them—something that he cannot see or account for right then and there—he becomes temporarily shocked from sheer fright. On the battlefields, in the midst of artillery fire, it is comparatively the same. Today the common term used is 'psychoneurosis.' Symptoms of combat fatigue are similar, and practically all 'psycho' patients are curable with medical science, proper care and treatment over a period of time. However, each patient requires a different treatment. No two cases are identical by any means. Fanatically minded men, who incessantly read the Bible and talked religion and put themselves through hours of prayer

ritual and rite, were segregated from the political-minded (of which I was classified); and, last, were men who wouldn't talk or answer questions intelligently and who temporarily had complete loss of memory.

"It was Memorial Day, May 30, when finally I embarked on an Army transport en route to San Francisco and the States. The homeward voyage was made on a former luxury liner jammed from stem to stern with war-wounded of all descriptions. What used to be the smoking lounge aboard ship had been turned into a steel-screened cage. It was there I was packed in with half a hundred other patients for the return trip. From hospital to ambulances and then to dock and ship, we were handled like prisoners of war, literally speaking, and throughout the entire movement I never once stopped talking.

"The reader may wonder how I ever found so much to talk about day in and day out. I, too, have been wondering the same thing. But, being fortunate in having a marvelous memory, I do recall that I covered every subject imaginable in my revision of world affairs, including the lack of sexual relationships for starving, fighting soldiers overseas. I contended that if the Allies marched a hundred thousand American (female) bathing beauties in front of the German or Jap armies, the war would end instantly. I criticized the government severely for not thinking of it as an answer to warring problems. To every new officer or ward boy I met I introduced myself, and then told them when the war would end and promised that all fighting men would have plenty of women to love, prosperity, long life and happiness for the rest of their days on earth—after 'June 30!' . . .

"I stressed the thought that, when we got back home, we men would have to stick together and make certain the women got off their high throne of independence and went back to work in the kitchen, doing housework and raising babies, where they rightfully belonged. I cautioned that if we permitted them to continue dominating men (politicians' wives not exempted) and demanding a price for their affections before and after marriage, a country or a nation, or an individual man's life, wouldn't be worth the sacrifice military men all over the world had been paying. For that remark I was cheered profusely by all males within the sound of my voice.

"Arriving in San Francisco, we were herded from ship to ambulance and then for a drive through the city to another Army hospital. When an attendant asked me my home address, I merely shrugged my shoulder and said, 'Why, young man, I'm on my way to the White House, Washington, D. C., where I will visit the President for several months.' I then went on to elaborate on making a report to the President about conditions overseas. The attendant lent a willing ear until I asked him where the photographers were. I expected my picture to be taken at once. He smiled and assured me he would go and get them as soon as my papers were made out in full. I, of course, never saw him again, but invariably my mind always seemed to blossom forth with an excuse for things not materializing the way I first expected. However, June thirtieth was one day I knew positively—everything would turn out exactly the way I had prophesied a thousand and one times.

"Our quarters the first night back in good old U. S. A. was a large cement building, resembling a real penitentiary. There was a maze of corridors, cell blocks, stairways with iron gates at both top and bottom, thick, barred windows and closed-in sleeping wards. The atmosphere was frightening to all, especially when one could easily hear the nonsensical chatter of patients locked up in cell rooms and occasional screams and banging of doors and walls throughout the building. Escape was nigh impossible.

"My fears were somewhat relieved when I set eyes on our night nurse—a beautiful girl with coal black hair and saucer-like, big blue eyes. She was dressed immaculately in white and possessed an odor of sweet fragrant perfume as she flitted by the beds counting her patients. I fell in love at once, and, although I didn't know her name, I called her Louise! A couple days later, in my mind we had been married by God himself, and thereafter I referred to her as 'my wife.'

"It must be remembered, as the days came and went, I kept 'talking' continuously and paced to and fro burning up valuable body energy. Writing letters to notable people all over the world also continued without let-up. (Fortunately for me, they were not mailed, as all letters written by 'psycho' patients were obviously censored and, if found not to be sensible, were destroyed.) My weight remained approximately 132 pounds, when it should have been at least 150 pounds. My appetite was only fair, and I felt extremely nervous while eating; quite frequently I'd skip a meal or two, with the idea in mind that I was far too busy and too important a person to take "time out" for such a trivial matter as gaining nourishment. I smoked cigarets in chain fashion, one right after the other, which amounted to two, and sometimes three, packages daily, whereas normally I smoked less than a full pack a day.

"With the coming of the latter part of June, I was put on a Red Cross train with other patients and moved inland to a hospital near Sacramento, Calif. All during the trip I talked about June 'thirtieth' and quite nonchalantly promoted myself to the rank of a five star general in command of all armed forces. Prior to my self-made appointment, I was 'Jesus Christ' in person, the most intelligent human being in the world, and I didn't hesitate to introduce myself as such.

"The time was close to midnight on a Thursday evening when I arrived by bus from the railroad station at the general hospital in California. The hospital had been open only a few months, and immediately I was under the impression that I was on an inspection tour of new hospitals. While en route on the train, I had written in pencil that I was a five star general and the supreme head of the general staff of the United States Army.

"At the entrance to our new ward I was met by a nurse and a major, whom I later learned was formerly in civilian life a famed psychiatrist of a hospital in New York city. I approached him and shook hands, telling him who I was and that I was taking command of the hospital the following day. He smiled with dignity and proceeded to help me change clothes, because the convalescent suit I was wearing was the property of the hospital in San Francisco. Again I wish to bring to the reader's mind that everything I said and did made sense to me. . . . If the people whom I came in contact with had refused to agree with me, I would have easily wound up in a strait jacket.

"Friday, June 'thirtieth' dawned a beautiful day for every one—but me! I couldn't understand why it was no different than most days. I expected much joy and celebrating; instead, doctors, nurses and ward boys were going around as usual performing their daily tasks. I pleaded for radio news, or a newspaper, but nobody seemed to have the news I so eagerly awaited. Needless to say, by Saturday noon I was deeply depressed. But the next week was decidedly one of reassurance to myself, for I sincerely believed the war had ended on Friday and that it was being kept a military secret by traitors to our nation and by greedy politicians who wouldn't tell the world the truth. I knew that if I could only get before a radio microphone I'd set the world straight.

"One morning I was awakened by a ward boy and a nurse. The ward boy held a hypodermic needle in his hand. 'It's orders,' he said. I bolted upright in bed and exclaimed, 'I refuse! You aren't going to puncture me with that needle,

because I'm different than any other human being. I have water veins and blood veins in my system and also air veins. No one else in the world has air veins. If you puncture them, I'll die.' The ward boy grinned and handed the needle to the nurse. She shook her head, and they both left the room. A few minutes later another nurse held the needle in her hand. I was out of bed and on my feet ready to attack the needle. I wanted to knock it out of her hand, but as I made the effort, from out of nowhere came three other ward boys and I found myself suspended in midair and the nurse had already given me a shot in the arm.

"In no time at all I began to feel weak, and back to bed I went. My mouth became dry and I thirsted for ice water, which was given to me whenever I called for it. Two hours later I was starving hungry; but I was refused food until 10 o'clock in the morning. In the afternoon I was given another shot in the arm, and again I thirsted for ice water and f-o-o-d! I was soon told that the shots I was being given were insulin! And that they would continue twice daily for a period of one month, at least. The third day my hunger became unbearable. I made attempts to steal food from the refrigerator and even snatched a piece of toast from another patient's mouth and ate it. From 7 o'clock until 10 o'clock each morning seemed an eternity. When I finally did eat breakfast, it consisted of six boxes of dry cereal, four bottles of milk, toast, eggs, sausages, coffee and fruit. One morning a half grapefruit tasted so good I ate the rind and all. Gradually I began to put on weight until I was averaging 3 or 4 pounds every other day. I ceased to talk so much and spent more time sleeping.

"As each day went by, the insulin was increased in the amount of units they were giving me, until I finally went into what is called subshock! The shock usually hit me about an hour before breakfast. I would be half asleep most of the time, when suddenly something seemed to rush through my brain, 'lifting' my head and, at the same time, spinning it around and around. I would struggle within myself to remain conscious and could feel my body vibrate from head to foot. I could see 'double' and sometimes 'triple' of every one and everything near me. Presently I would hear the voice of the ward boy, the nurse or the doctor telling me to swallow the 'orange juice and sugar' they were attempting to get into my mouth. Momentarily, I seemed to be in different worlds, constantly trying to come back to reality. Trying vainly to cling to familiar scenes and familiar faces. Instinctively I knew I was losing all my equilibrium. But as soon as the orange juice and sugar settled in my stomach, I snapped out of it and was ready for more food.

"After ten days of insulin, my mind began to clear. I realized my thoughts and actions of the past had been wrong—totally wrong! On the fifteenth day of insulin I fully realized the shape I had been in, and I cleared up for good. It was then I discovered that insulin eats up the sugar content in one's body and blood stream, creates an appetite and subshocks the mind into normalcy. My weight jumped from 132 to 165 pounds in thirty-one days. And since coming off the insulin treatments I have held that weight, a little over a month and a half.

"I have nothing but the greatest praise for the doctors, nurses and ward boys of the United States Army Medical Department, and for science, for their patience, tolerance, and sympathetic understanding toward a war-torn mind and body of soldiers returning from combat zones. And to think that, in this modern world of science, one can be put back in good health mentally and physically in such a short space of time—it is indeed a modern miracle of man."

CASE 5.—A man aged 31, with eight months of service, was admitted on Sept. 20, 1944, with a diagnosis of "psychoneurosis, mixed type, severe."

Relevant History.—The father was an architect and contractor. The mother was nervous and "inclined to be hysterical." She had had a nervous breakdown. Both parents were "very moral and puritanical—emotionally cold." The patient disliked both of them. He was born in suburban East Hampton, Mass., the younger of 2 siblings (the sister was fifteen years older than the patient). His was an instrument birth, with the early feeding complicated by the mother's inability to provide adequate milk for breast feeding. When the patient was 12, the family moved to Washington, D. C. There paralysis (psychosomatic) of both arms developed, the condition lasting a year and a half. He had had severe headaches as a child. He began school at 5, lost a half-year because of his "paralysis" and completed high school at the age of 18. He attended college for two years and business college for one year and completed his undergraduate work in 1935, at the age of 23, with the degree of Bachelor of Arts. He attended the University of California from 1937 to 1939, receiving the degree of Master of Arts. In 1940 he began work on his Ph.D. degree and had completed it except for his thesis and examinations. He took part in no extracurricular activities and had only a few friends. He held a secretarial job and lectured. Heterosexual adjustment was adequate; he was married, but both he and his wife disliked children. He was once arrested on a charge of drunkenness and disorderly conduct and paid costs. His use of alcohol was moderate, but it had increased since his entrance into the Army. He stated that whenever possible he got "stinko." He was not interested in the Army—"You always run up against a brick wall of regulations." He stated that his personality varied from extrovertive to introvertive; he was not interested in competition and had been overprotected at home. For fifteen years he had been concerned about his back. Since induction he had been tense, anxious, insecure and emotionally unstable.

Present Illness.—The patient stated that he had no interest in being in the Army, that "after spending fifteen years in Washington and listening to all the ballyhoo there" he just could not see himself in the Army. Since induction he had made no special effort to adjust to Army life and had been constantly frustrated by regulations, "non-coms" and officers. As a result, he had become increasingly insecure, irritable, moody and depressed.

Physical Examination.—His blood pressure was 135 systolic and 80 diastolic. The findings were normal.

Special Examination.—A roentgenogram of the chest was normal. Roentgenograms of the lumbar and sacral portions of the spine showed slight changes; the lateral view revealed mild kyphotic angulation at the level of the first and second lumbar vertebrae and what appeared to be minor narrowing of the anterior border of the body of the first lumbar vertebra. Roentgenograms showed minor haziness of the frontal sinuses; marked thickening of the lining membranes of both maxillary sinuses, more pronounced on the right, and some cloudiness of the posterior ethmoid cells.

Mental Status.—The patient was ambulatory. He was alert and tidy but was depressed, discouraged, complaining, irritable, resentful, cynical and sarcastic. He slept poorly; concentration was poor; memory was becoming poor, and he tired easily. He had no hallucinations, delusions or persecutory ideas. He feared the stupidity of his superior officers. Somatic complaints were backaches, headaches due to sinus involvement and occasional swelling of the left knee. The symptoms of nervousness included tension, instability, anxiety and insomnia.

Course in Hospital.—The patient was placed under routine insulin subshock therapy, the period of treatment being twenty-two days, the maximum dose 160 units and the stay in the hospital fifty-eight days.

Final Diagnosis.—The diagnosis was psychoneurosis, mixed type, severe, in a cyclothymic personality, manifested by tension, anxiety and depression.

Condition.—The condition was improved.

Disposition.—The patient received a medical discharge.

Comment.—This patient presented a difficult problem in psychotherapy. He was highly intelligent, egotistical and sarcastic and had an attitude of superiority. After much discussion with him, he reluctantly agreed to take insulin therapy. A spontaneous autobiographic account of his experience follows.

"EFFECTS OF INSULIN TREATMENT"

"I knew at the time I was sent to the insulin ward that I was well on the way into another depression. I also knew that my periods of depression varied in intensity, and I was afraid that conditions in the ward would intensify this depression. But at no time during my three weeks and three days on the ward did I suffer the depths of depression that I have known under ideal conditions at home.

"During the first three days and nights I had no sleep (sleeplessness always accompanies my periods of depression and of elation). I was afraid that I was in for another week or two of sleeplessness, but on the fourth day I was 'shocked' slightly, and that night I slept for six hours.

"However, I was still skeptical of the treatment. Perhaps I wasn't going to have as bad a depression as I feared. The radio still bothered me, and I still avoided the other patients. And the thought persisted—'How can any drug help the product of generations of New England neurotic ancestors?'

"At the end of the first week I had gained 10 pounds. I was beginning to find the other patients good company. I wondered why I had been so concerned with problems to be met in civilian life. In short, I realized how seriously ill I had been and knew that the insulin had checked a bad period of depression.

"Frequently in the past I have come out of a depression, only to find myself in an equally bad period of preposterous elation. In my second week of insulin treatment I began to feel so well that I feared a period of playing the fool. But I continued to sleep well and to feel more peaceful than I have felt since my induction into the Army. Even though I felt better, I didn't have to be a buffoon or the life of the party to impress people with my cleverness. The third week was a reaffirmation of my peacefulness and steadiness. Even the joy of going for a walk on the day I was released from the insulin ward did not disturb my equilibrium. I returned from the walk and slept an hour.

"My amazement at the effects of insulin treatment is equaled only by my amazement at the equanimity of the physicians who bore my insults during the first week. My deepest gratitude is for the knowledge of the efficacy of insulin, because my fear of depression was almost as painful as the depressions themselves; that is, I can now cease to worry about them, for I shall unhesitatingly have the treatment again when or if my depressions recur."

CASE 6.—A technician fifth class, aged 30, with one year and ten months of service, was admitted on Oct. 15, 1944, with the diagnosis of severe psychoneurosis, anxiety state.

Relevant History.—Two paternal great uncles died in a psychiatric hospital, the nature of the psychosis being unknown. The father, aged 59, drank excessively

for three or four years in the 1920's but was a total abstainer at the time of this report. He was domineering, even brutal at times. The mother was introvertive, nervous and a chronic worrier. The family lived on a farm, and a pattern of dependency had been developed by the parents. The patient was the fifth of 9 siblings; birth was normal. When about 6 years of age, he suddenly had attacks in which he would wake up from sleep and yell loudly, acting as though something were after him; he would appear unconscious, and cold water would bring him out of it. These attacks lasted for four years. He had frequent temper tantrums and was extremely afraid of water and of the dark; he had had enuresis up to the age of 8 years. He had always chewed his finger nails. He had always been conscientious and serious minded; he was extremely sensitive and would cry over small things. His father said that he worked harder than any of the other children on the farm. While other siblings resented the father's domination, the patient did not. He had always been nervous and a worrier, and was strait-laced, moralistic and religious. He was frail and had always given a great deal of attention to his health. The family history indicated a great deal of insecurity and instability and provided the framework for the patient's present illness.

Present Illness.—A few days after his arrival in Oahu the patient began to complain of pain in the lower part of the back, extending into the legs, and of numbness, tingling of the legs, restlessness and tenseness. These symptoms increased in intensity and were accompanied with depression and tremulousness. He was hospitalized on May 3, 1944, observed for six weeks and then returned to duty. On his being returned to duty, his pain became worse, and he began to exhibit a stammer, which gradually became worse. He was rehospitalized on July 22 and transferred to an Army general hospital on August 8. In all hospitalizations the diagnosis was severe psychoneurosis, anxiety type. However, the patient refused to accept this explanation. His anxious state of mind was aggravated by the death of a soldier in his organization at about the same time that his backaches became severe. He had been greatly concerned about a small lesion on his penis, which cleared rapidly with medication while he was still in the States. However, this had reappeared in a larger and more aggravated form shortly before he embarked for overseas. He felt that his aches were further symptoms of the disease. Evidently, separation from his wife and home were the precipitating factors in the patient's illness, but he resented any intimation regarding his dependence or homesickness.

Physical Examination.—The blood pressure was 125 systolic and 70 diastolic. The physical condition was essentially normal except for irritation of the skin of the face, where he had picked at it constantly.

Special Tests.—A routine blood count, urinalysis and roentgenologic studies of the chest revealed nothing remarkable.

Mental Status.—The patient was extremely tense, anxious, restless and preoccupied. Judgment and insight were impaired. He was hostile when questioned. He continuously picked at his face and was emotionally unstable and impatient. There was no evidence of any psychotic content.

Course in Hospital.—He was placed under routine insulin subshock therapy for twenty-three days, the maximum dose being 175 units and the total stay in the hospital sixty days.

Final Diagnosis.—The diagnosis was psychoneurosis, mixed type, severe, manifested by tremulousness, anxiety, syphilophobia and somatic complaints without organic basis.

Condition.—His condition was improved.

Disposition.—The patient received a medical discharge.

Comment.—The patient had a severe, long-standing psychoneurosis and received considerable symptomatic relief from insulin subshock therapy. Subsequent psychotherapy seemed to help in the development of insight; he was referred to a civilian clinic for further treatment.

CASE 7.—A private aged 21, in the Army Air Forces, ground crew, with one year and nine months of service, was admitted on Sept. 5, 1944, with a diagnosis of dementia precox, paranoid type.

Relevant History.—The patient was the fifth of 7 siblings; he weighed 13 pounds (5,896 Gm.) at birth. He talked in his sleep and said that he had been nervous since the age of 10. He stopped school in the senior grade of high school, at the age of 17, because of a sick spell, in which he lost his voice for about a month. After leaving school, he went to work as a handy man around the estate of a retired lawyer and later did odd jobs for his father and brother. He gave the usual history of masturbation, with no excessive worry. He had had heterosexual relations since the age of 16, with no homosexual tendencies. He had had no serious conflicts with the law; his hobbies were cartooning and various types of art work. He had done a good deal of drinking, getting drunk about once a week. His father and mother appeared to be normal, well adjusted, affectionate people, and, according to the patient, there was no ancestral psychopathy, either direct or collateral.

Present Illness.—The patient was admitted to the hospital for the first time on May 24, 1944, with a mild cerebral concussion, after which he became seclusive and paranoid and made a suicidal attempt. Later he showed much anxiety, drew bizarre pictures and was evacuated to the United States with the diagnosis of dementia precox, paranoid type.

Physical Examination.—The condition was essentially normal, with a blood pressure of 130 systolic and 85 diastolic. There was no neuropathology.

Laboratory Examinations.—Laboratory studies revealed nothing abnormal.

Mental Status.—The patient was ambulant, seclusive and preoccupied, with some manifestations of overt anxiety. He was underproductive but coherent and relevant. His mood was depressed, resentful and discouraged, with evidence of considerable tension. He felt that he was being watched and had the delusion that people were trying to pin something on him; he misinterpreted and believed that the ventilators in the ceilings were dictaphones; he felt that people thought that he was queer because of his drawings and admitted that while overseas he heard voices of an accusatory nature. The sensorium was clear, with intellectual faculties adequate. Judgment was poor, although he realized that something was wrong.

Course in Hospital.—The patient was given insulin subshock treatments for nineteen days, the maximum dose being 200 units and his total stay in the hospital thirty-two days.

Final Diagnosis.—The diagnosis was psychosis, unclassified, acute schizophrenic reaction.

Condition.—His condition was improved; he was less tense, with loss of much of his delusional content, and showed more insight and better judgment.

Disposition.—The patient was discharged by transfer to the veterans' administration facility.

Comment.—We should have given this patient more insulin treatment, for he had only ten "reactions"; also, we should have kept him another month, for he was improving, rather than transfer him to a veterans' hospital. Two weeks after arriving at the latter, he was placed on a ninety day trial visit and was discharged at the expiration of that period, with a diagnosis of dementia precox, hebephrenic type, in partial remission.

CONCLUSIONS

1. Intensive insulin subshock therapy (adequate subshock reactions twice a day, seven days a week, for three weeks) should be used in treatment of all psychoses with schizophrenic symptoms.

2. Intensive insulin subshock therapy should be used with all psychoneurotic states of the severe anxiety-tension type, psychoses with features of depression and psychoses of mixed type.

3. Psychoses which do not respond satisfactorily to intensive insulin subshock therapy should be given a course of at least twelve electric shock treatments (one treatment three times a week); this will increase the over-all rate of improvement and remission to 90 per cent.

4. Intensive insulin subshock therapy is a relatively safe procedure and can be carried out in a group setup in which from 20 to 30 patients are cared for by two nurses and five attendants. This personnel can be trained easily to recognize the signs and symptoms of reaction to insulin and the proper point at which to terminate the insulin subshock reaction by oral administration of sugared orange juice or intravenous injection of hypertonic dextrose solution. The proper point at which to terminate the subshock reaction is when the patient can barely be roused or shows evidence of impending convulsion.

ETIOLOGY OF OPTOCHIASMATIC ARACHNOIDITIS

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IN SPITE of the increasing number of cases of optochiasmatic arachnoiditis reported in the literature and the general recognition of such a condition at operation, the etiologic agent in many instances remains obscure.[1]

Optochiasmatic arachnoiditis is defined as an abnormal thickening of the arachnoid in the region of the optic nerves and the optic chiasm. The process frequently extends to neighboring structures, in particular to the region of exit of both third nerves, and may reach the caudal portion of the pons, in which case the term basilar arachnoiditis is more appropriate. In the older literature the same condition goes under the name of chronic basilar meningitis.

Fine films of arachnoid are normally present, forming the chiasmatic cistern. In cases of optochiasmatic arachnoiditis there are solid bands of the arachnoid, which insert either on the optic nerves or on adjacent structures, such as blood vessels. Or there are "aprons" of thickened arachnoid, hiding completely from view the optic nerves and chiasm.

The condition gives rise to the chiasmatic syndrome of primary atrophy of the optic nerve and has been considered an indication for surgical intervention. Other causes producing a similar syndrome, according to Cushing,[2] are suprasellar meningioma, pituitary adenoma, craniopharyngioma, glioma of the chiasm and suprasellar aneurysm.

Optochiasmatic arachnoiditis has a varied origin, which in most cases is not known. Vincent and his collaborators,[1] who seem to have had the largest operative experience with this condition, give the following causes of its development: (1) infections of cavities of the face, (2) cerebromeningeal infections, (3) trauma and (4) rare and poorly understood causes.

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1. Bollack, J.; David, M., and Puech, P.: Les arachnoidites opto-chiasmatiques; Étude ophtalmologique et neuro-chirurgicale, Paris, Masson & Cie, 1937.

2. Cushing, H.: The Chiasmal Syndrome of Primary Optic Atrophy and Bitemporal Field Defects in Adults with a Normal Sella Turcica, Arch. Ophth. **3**:505 (May); 704 (June) 1930.

MATERIAL AND METHOD

In this communication are reported the results of an anatomic study which had as its aim the determination of factors which tend to produce an abnormal thickening of the arachnoid at the base of the brain and ultimately lead to what may be termed optochiasmatic arachnoiditis. In 400 consecutive necropsies, special attention was paid to the status of the arachnoid in the optochiasmatic region. The necropsy material included cases of trauma to the brain, encephalitis, the various types of neurosyphilis, rheumatic fever, intracranial neoplasms and multiple sclerosis. All these conditions have been given as agents which may produce optochiasmatic arachnoiditis. In addition, brains with Schilder's disease, Pick's disease, hydrocephalus and severe cerebral atherosclerosis and the brains of persons from a very high age group were included in the study. There was available a complete serologic study of the blood and the spinal fluid in every case. In removing the brains, the utmost care was exercised not to disturb the relation of the arachnoid to its neighboring structures. In every instance a photograph was taken to supplement the descriptive notes.

ETIOLOGIC FACTORS OF OPTOCHIASMATIC ARACHNOIDITIS

I. INFECTIONS OF CAVITIES OF THE FACE

In my material, there were no cases of infections of cavities of the face and other areas adjacent to the brain (sinuses, middle ear and mastoid). In Vincent's clinic,[1] such infections were the cause of optochiasmatic arachnoiditis in 10 out of 66 cases. The French observers were inclined to believe that sinal infections can maintain a meningeal reaction in the same sense as does an otitic infection. Cushing,[2] however, had long been skeptical as to the relation of inflammatory processes in the paranasal sinuses to thickened arachnoid of the chiasmatic cistern. He emphasized that, to his knowledge, no pathologist had ever been able to demonstrate any histologic evidence of disease in the supposedly hypertrophic mucous membrane and spongy bones which were removed from the ethmoidal region of patients with atrophy of the optic nerve. He went on to say that frank suppuration of the sphenoidal or ethmoidal cells may produce paracentral scotomas with disturbances of vision, but that one should be cautious in ascribing unexplainable atrophy of the optic nerve to undemonstrable infections in the schneiderian recesses.

On the other hand, thickening of the arachnoid which follows closely otitis media is one of the best established types of cisternal arachnoiditis.[3]

Infections of teeth have been incriminated. Craig and Lillie[4] reported a case of a chiasmatic syndrome due to arachnoiditis following an abscess of the lower right molar teeth of six months' duration. Within a few hours after the second lancing of the abscess the patient became almost completely blind in one eye. When at operation, five months

3. Horrax, G.: Generalized Cisternal Arachnoiditis Simulating Cerebellar Tumor: Its Surgical Treatment and End-Results, Arch. Surg. **9**:95 (July) 1924.

4. Craig, W. M., and Lillie, W. I.: Chiasmal Syndrome Produced by Chronic Local Arachnoiditis; Report of Eight Cases, Arch. Ophth. **5**:558 (April) 1931.

later, the right frontal lobe was elevated, dense adhesions were observed surrounding the chiasm and the optic nerves, and the diagnosis of an inflammatory lesion of the chiasm was made. Autopsy five days later showed basilar arachnoiditis with thick adhesions around the optic chiasm. Unfortunately, there was no microscopic examination of the chiasm.

II. CEREBROMENINGEAL INFECTIONS

Encephalitis.—Of the infections of the brain, the various types of acute and chronic encephalitis have been mentioned as a cause of optochiasmatic arachnoiditis. At necropsy Craig and Lillie [4] observed basilar arachnoiditis in a case of encephalitis. Although the chiasmatic syndrome was attributed exclusively to the arachnoidal adhesions, it is possible that the encephalitic process may have led to demyelination of the visual pathways, contributing to the disturbance of vision. The optic chiasm and optic nerves were not examined microscopically in this case. A combination of such lesions was present in another case reported by Craig and Lillie,[4] in which basilar arachnoiditis was associated with encephalitis and cyst formation in the optic chiasm. On the other hand, chronic encephalitis may produce the symptoms of "pseudotumor cerebri," which is usually ascribed to basilar arachnoiditis, without any evidence of thickening of the arachnoid at the base of the brain.[5]

In my own material were 9 cases of von Economo's (lethargic) encephalitis, in which the patients died many years later with postencephalitic parkinsonism. The arachnoid in the interpeduncular space was normal in all instances. In 1 of these cases there was an unexplained atrophy of the optic nerve. The optochiasmatic arachnoid, however, was not thickened.

Horrax [3] gave lethargic encephalitis an important place in the causation of cisternal arachnoiditis. Twelve of his 28 cases of the subacute or chronic form were observed in 1920, one year after the epidemic of influenza, at a time when many cases of lethargic encephalitis occurred.

Demyelinating Encephalitic Diseases (Multiple Sclerosis, Schilder's Disease, Encephalomyelitis Disseminata).—In multiple sclerosis, it has been surmised that the same mechanism which produces plaques in the brain and the optic nerves may cause optochiasmatic arachnoiditis. There were 4 cases of multiple sclerosis in my material. In none was there an abnormal thickening of the optochiasmatic arachnoid, in spite of the fact that in 2 instances, on histologic examination, huge plaques were observed in the optic chiasm and in the intracranial portion of both optic nerves.

5. Bailey, P.: Contribution to the Histopathology of "Pseudotumor Cerebri," Arch. Neurol. & Psychiat. **4**:401 (Oct.) 1920.

In the 1 case of Schilder's disease there was only slight thickening of the optochiasmatic arachnoid, which could still be considered within normal limits, although the demyelinating process had extended into the chiasm and the optic nerves. In the 1 case of encephalomyelitis disseminata there was no arachnoidal thickening at the base.

Of greatest interest was a case of Pick's disease with atrophy of the optic nerve. Autopsy revealed slight thickening of the optochiasmatic arachnoid. The atrophy of the optic nerve, however, was due to cavity formation in both optic tracts, which was followed by secondary degeneration of the nerve fibers.

Purulent Meningitis.—One might assume that the acute, purulent meningitides furnish an important background for the development of optochiasmatic arachnoiditis. Oddly, this is only rarely the case.[1] The accumulation of purulent material in the chiasmatic region, which at times may produce sudden blindness,[6] is obviously followed by complete absorption, without leading to thickening of the optochiasmatic arachnoid.

How difficult and misleading may be the clinical interpretation in such cases is illustrated by the following instance:

An infant, 3 months of age, had cerebrospinal meningitis, which was followed by extreme hydrocephalus, unilateral atrophy of the optic nerve and diminished vision in the other eye. It was argued that the loss of vision was the result of optochiasmatic adhesions in the wake of purulent meningitis. Necropsy revealed only slight thickening of the arachnoid at the base of the brain, which did not exceed normal limits. The visual disturbance was due to pressure of the distended third ventricle, which flattened the chiasm, with resulting atrophy of some of the chiasmatic fibers.

Syphilitic Optochiasmatic Arachnoiditis.—On the other hand, syphilis not infrequently maintains a chronic, and usually asymptomatic, basilar meningitis, which in the course of years may lead to optochiasmatic arachnoiditis. This is easily explained by the tendency of the syphilitic organism to involve more readily the meninges than any other structure of the brain.

It remains unexplained, however, why in some cases of neurosyphilis even of the same type, dementia paralytica, for example, there is pronounced arachnoiditis at the base of the brain (fig. 1 *A*), whereas in other cases of dementia paralytica the chiasmatic region is entirely free from arachnoidal adhesions (fig. 1 *B*). Yet in the latter, microscopic examination discloses likewise a slight round cell infiltration at the base of the brain, as well as in the pia of the optic nerves and chiasm. This observation is of the greatest significance in the pathogenesis of syphilitic

6. Schottmüller, H.: Ueber Meningitis cerebrospinalis epidemica, München. med. Wchnschr. **52**:1729, 1905. Lewis, P. M.: Ocular Neuropathies and Amauroses in Meningococcic Meningitis, South. M. J. **26**:729, 1933.

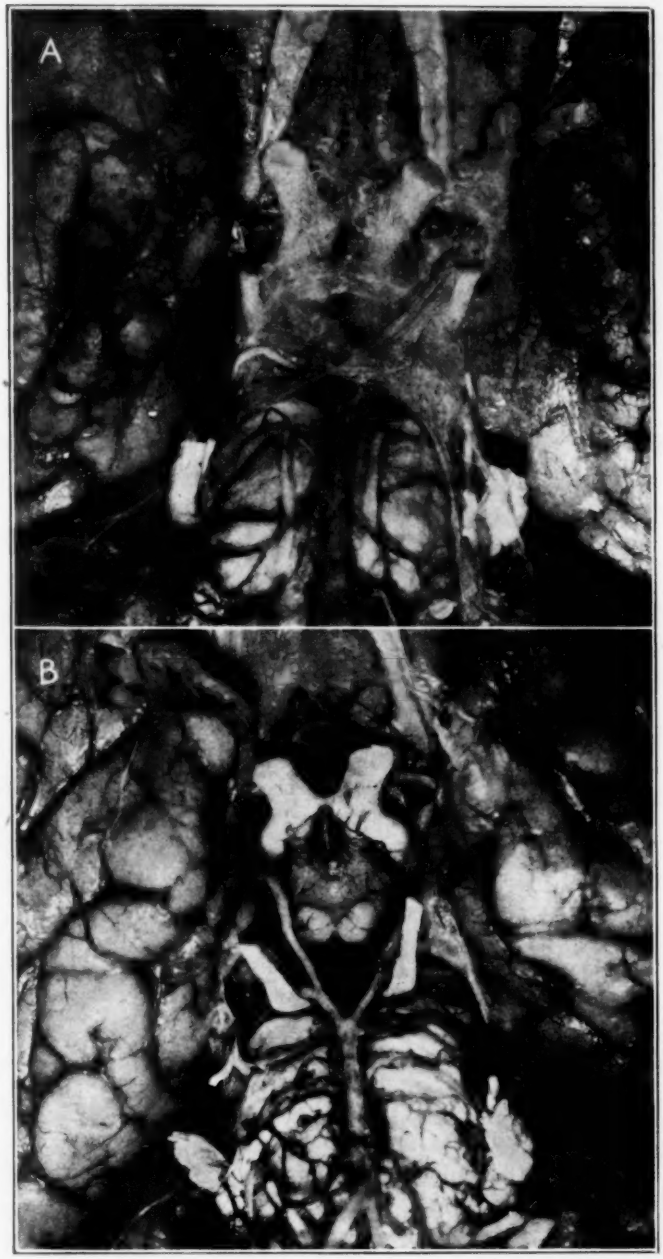

Fig. 1.—*A*, syphilitic optochiasmatic arachnoiditis (asymptomatic) in a case of dementia paralytica. *B*, normal appearance of the chiasmatic region in a case of dementia paralytica. In spite of the "normal appearance" on gross inspection, microscopic examination revealed a mild degree of syphilitic basilar meningitis.

primary atrophy of the optic nerve, indicating the presence of mild basilar meningitis, although the base of the brain may grossly appear entirely normal.

Significance of Pleocytosis in Relation to Syphilitic Optochiasmatic Arachnoiditis.—One might assume that the number of cells in the spinal fluid would be the decisive diagnostic factor in determining whether or not basilar arachnoiditis would develop in a case of neurosyphilis. This question received especial investigation because of a recent statement by Lange and Harris,[7] who expressed the opinion that the number of cells in the spinal fluid provides a quantitative expression of the inflammation in the meninges and perivascular spaces. This statement should be accepted with reservation, for in a number of cases this assumption does not hold good when checked by histologic examination. For instance, in my material were 2 cases of dementia paralytica with 245 and 205 cells per cubic millimeter, respectively, in which autopsy revealed a normal arachnoid at the base of the brain and only a slight degree of meningeal turbidity over the upper aspect of the frontal lobes. On the other hand, a patient with untreated dementia paralytica with only 7 cells per cubic millimeter had definite arachnoidal thickening in the interpeduncular space.

In 10 consecutive cases of dementia paralytica with an entirely normal base of the brain the mean cell count was 77 cells per cubic millimeter, and in 10 other cases of dementia paralytica with optochiasmatic arachnoiditis the mean cell count was 100 per cubic millimeter. Of the cases in which the base of the brain was normal there were 2 with 205 and 245 cells per cubic millimeter, respectively, and 2 with a cell count of less than 10 per cubic millimeter. In the cases of optochiasmatic arachnoiditis the 2 highest cell counts were 155 and 600 per cubic millimeter, respectively. In the group with optochiasmatic arachnoiditis were also 2 cases with a cell count below 10 per cubic millimeter. In short, the cell count of the spinal fluid is of no decisive diagnostic value in the question whether or not optochiasmatic arachnoiditis is present in a case of neurosyphilis.

Frequency of Syphilitic Optochiasmatic Arachnoiditis.—The importance of syphilis in the causation of arachnoiditis at the base of the brain was emphasized by Vincent, Puech and Berdet,[8] who stated that in 2 out of 5 of their cases of optochiasmatic arachnoiditis the Wassermann reaction of the blood was positive. The frequency,

7. Lange, C., and Harris, A. H.: Interpretation of Findings in the Cerebrospinal Fluid: The Dementia Paralytica Formula and the Necessity of Its Quantitative Differentiation, Arch. Neurol. & Psychiat. **53**:116 (Feb.) 1945.

8. Vincent, C.; Puech, P., and Berdet, H.: Les arachnoïdites de la base du cerveau, Rev. d'oto-neuro-opht. **14**:418, 1936.

however, will vary with the concepts which various authors have of the clinical entity and limitations of this condition. Because of the frequency with which syphilis produces basilar arachnoiditis, one may safely say that arachnoiditis in a syphilitic patient is usually, although not necessarily, of syphilitic origin.

There are few, if any, anatomic studies of syphilitic optochiasmatic arachnoiditis. Most cases are reported from the clinical or surgical side. In Hausman's [9] study of syphilitic arachnoiditis of the optic chiasm a case was included in which autopsy showed a syphiloma in the right hemisphere, accompanied with gummatous meningitis at the base of the brain. In this case the concentric contraction of the visual fields was caused, in my opinion, by the gummatous infiltration of the chiasm rather than by constrictive arachnoidal adhesions.

Microscopically, syphilitic optochiasmatic arachnoiditis is observed to consist in thickening of the arachnoid to many times its normal thickness and diffuse infiltration with lymphocytes and plasma cells. The thickening of the arachnoid is augmented by proliferation of the fibroblasts and, to a lesser degree, by an increase in the arachnoidal lining cells.

III. TRAUMA

Next to an antecedent meningeal infection, trauma (fracture of the skull) has been mentioned as the most frequent factor in producing optochiasmatic arachnoiditis. In a series of 66 observations, the French authors found a history of trauma in 10 cases.[1]

In my material there were 9 brains with an old cerebral injury. In only 1 instance (fig. 2) was there a definitely thickened arachnoid at the base, beginning behind the chiasm and extending over the entire pons. The patient, at the age of 19, had been kicked in the temporal region by a horse, causing a huge laceration in the left centroparietal portion of the brain. There was no visual disturbance in this case.

The intensity of the trauma does not seem to play an important role in the production of traumatic arachnoiditis. One wonders why so few cases of optochiasmatic arachnoiditis were reported during the two world wars. By way of illustration, figure 3 represents the brain of a veteran of the Spanish-American War, who in 1898 sustained a shotgun injury to the left orbital lobe, without its leading to a pathologic thickening of the arachnoid at the base of the brain in the succeeding forty-four years of his life.

The role of trauma in the genesis of optochiasmatic arachnoiditis is far from clear. If there is direct destruction of the chiasmatic arachnoid by the injury or the formation of a hematoma at the base of the

9. Hausman, L.: Syphilitic Arachnoiditis of the Optic Chiasm, Arch. Neurol. & Psychiat. **37**:929 (April) 1937.

brain, the mechanism is more obvious. Then, there may be scar formation, and in the case of a hematoma the red blood cells in the meshes of the arachnoid may initiate stimulation and proliferation of the fibroblasts and of the arachnoidal lining cells, terminating in thickening of the arachnoid membrane.

A case which falls into this category was reported by Weill.[10] The patient presented symptoms of a suprasellar adenoma, which developed after a minor injury to the head in an automobile accident. There were bitemporal hemianopsia, diabetes, slight diminution of vision and roentgenologic changes in the sella turcica. Operation by Vincent did not disclose tumor but revealed optochiasmatic arachnoiditis with fibrous adhesions, passing toward the site of a traumatic scar in the cranium.

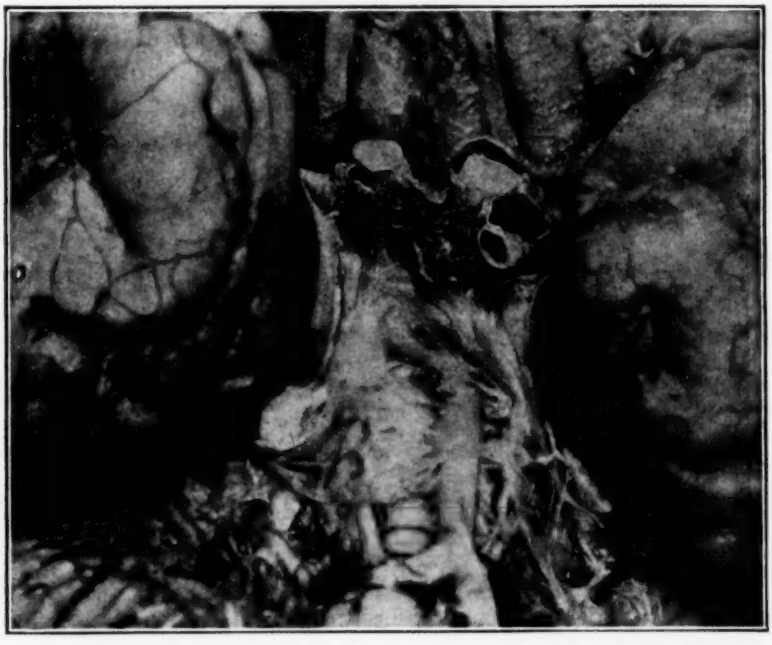

Fig. 2.—Traumatic arachnoiditis (asymptomatic), beginning behind the optic chiasm and extending over the pons.

Five other cases of trauma were described by Kenel.[11] After severe fracture of the skull, occurring in the frontal region in 2, there developed headaches, decrease of visual acuity and bilateral peripheral contraction of the fields. Fibrous bands of arachnoid were removed at operation. Exploration of the chiasm was followed by visual improvement, which in 2 instances was only temporary.

10. Weill, M. G., in discussion on Bollack, J.; David, M., and Puech, P.: Les arachnoïdites opto-chiasmatiques, Bull. et mém. Soc. franç. d'opht. **50**:198, 1937.

11. Kenel, C.: Cinq cas d'arachnoïdite optico-chiasmatique d'origine traumatique, dont quatre confirmés opératoirement, Ophthalmologica **96**:336, 1939.

IV. RARE AND POORLY UNDERSTOOD CAUSES

Rheumatic Fever.—Rheumatic fever has been said to cause optochiasmatic arachnoiditis. Puech and Mahoudeau [12] reported a case of a cardiovascular lesion in which recurring attacks of rheumatic fever were accompanied with symptoms of optochiasmatic arachnoiditis (loss

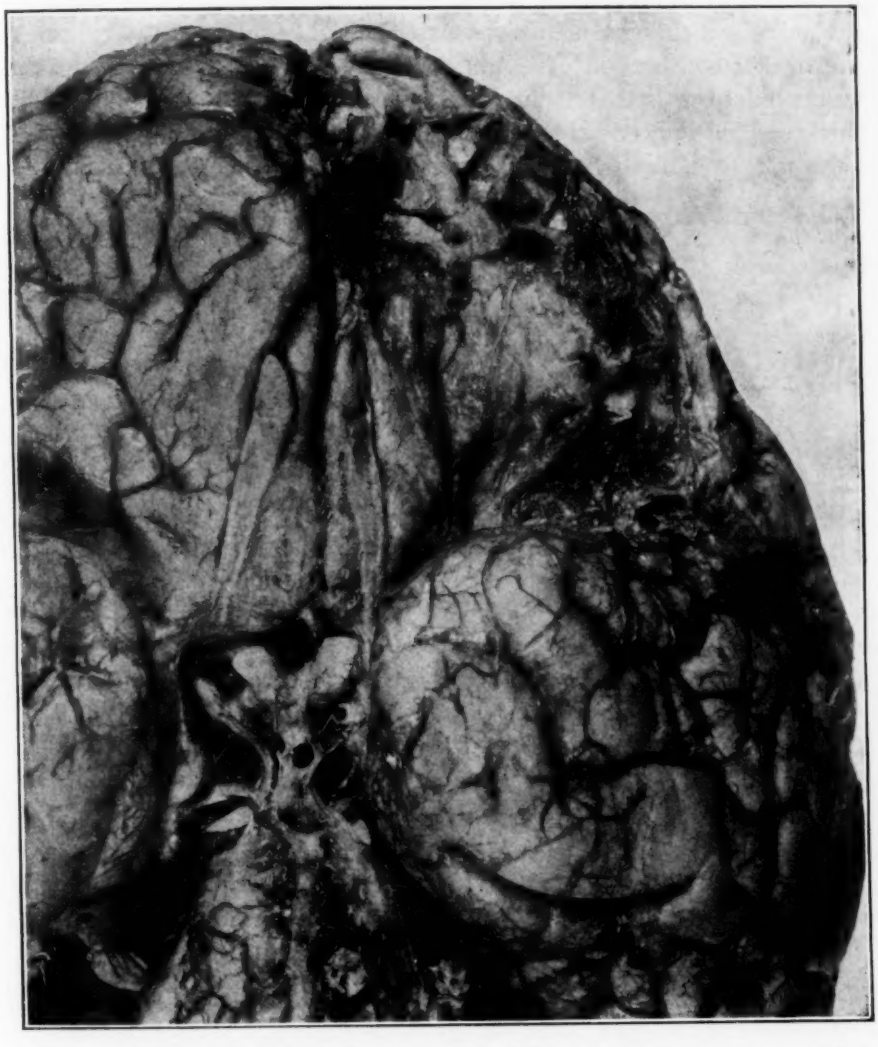

Fig. 3.—Shotgun injury of the left orbital lobe of forty-four years' standing. There is only slight thickening of the optochiasmatic arachnoid.

of vision). These authors insisted that a place should be reserved for rheumatic arachnoiditis besides the other manifestations of cerebral rheumatic fever.

12. Puech, P., and Mahoudeau, D.: Les arachnoïdites opto-chiasmatiques, Gaz. méd. de France, 1935, p. 101.

The involvement of the brain in cases of rheumatic fever has been studied extensively in the laboratories of this hospital.[13] A large series of such brains is available for the solution of the question whether or not rheumatic fever is likely to produce optochiasmatic arachnoiditis. Of 30 brains of persons with rheumatic fever, only 1 showed appreciable thickening of the arachnoid in the interpeduncular space. In this brain a band of arachnoidal adhesions passed harmlessly over the chiasm to the orbital convolutions (fig. 4). There was also fibrosis of the pia-arachnoid over both frontal lobes, which were matted together with thickened meninges. Here, obviously, was the end result of a former rheumatic meningitis, which had occurred in this case during the

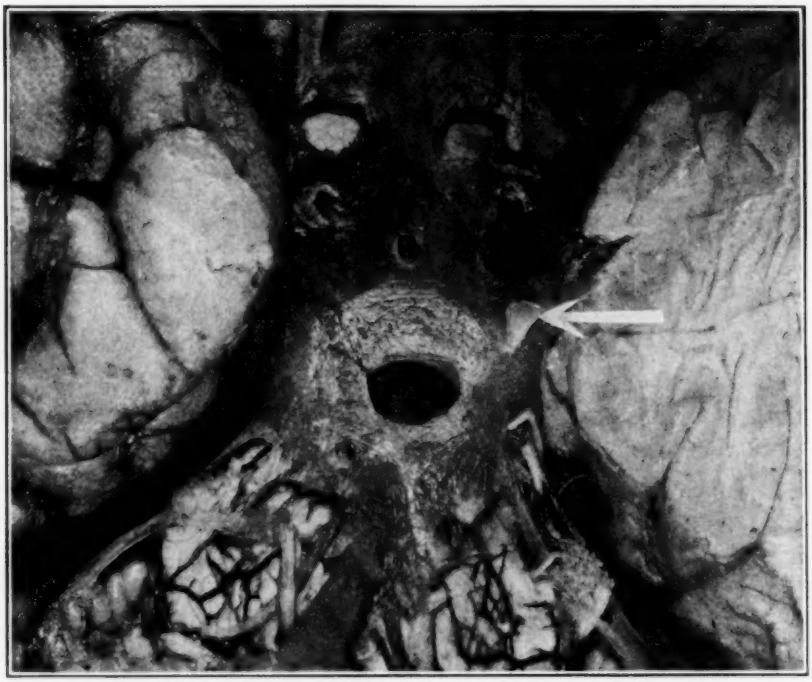

Fig. 4.—Asymptomatic optochiasmatic arachnoiditis of rheumatic origin. The arrow points to the left third nerve emerging through the thickened arachnoid.

patient's first attack of rheumatic fever. He died eleven years later of an acute recurrence of rheumatic fever. Microscopic examination of the thickened arachnoid disclosed only fibrosis, with absence of infiltrating round cells.

Involvement of the pia-arachnoid is rare in cases of rheumatic fever Poynton and Paine [14] observed meningitis, which was clinically asymp-

13. Bruetsch, W. L.: Late Cerebral Sequelae of Rheumatic Fever, Arch. Int. Med. **73**:472 (June) 1944.

14. Poynton, F. J., and Paine, A.: Some Investigations on the Nervous Manifestations of Acute Rheumatism, Lancet **2**:1760, 1905.

tomatic and chiefly basal in distribution, in a young patient who died while convalescing from an acute attack of rheumatic fever. The meningeal exudate consisted chiefly of lymphocytes.

More frequent than meningeal involvement in patients with cerebral rheumatic fever are obliterative endarteritic changes of the smaller cerebral vessels.[15] If visual changes develop[16] in a patient with rheumatic fever, one may assume that they are caused by an obliterating endarteritic process of a vessel in the visual pathways rather than by optochiasmatic arachnoiditis.

Cerebral Tumors.—Peritumoral arachnoiditis or arachnoidal cysts overlying a cerebral tumor are not infrequently encountered in operations for intracranial neoplasms. These arachnoidal cysts, if present, discharge the backed-up cerebrospinal fluid on removal of the tumor and can then no longer be recognized if the arachnoid was not thickened at the same time.

In a group of 13 cases of intracranial neoplasms, including meningiomas of the olfactory groove, pituitary adenomas and neurinomas of the cerebellopontile angle, areas of fibrosis in the immediate neighborhood of the new growth or in the optochiasmatic region were not observed at autopsy.

Cerebral Arteriosclerosis.—There were 26 cases of far advanced cerebral arteriosclerosis. In several instances the atheromatous internal carotid arteries had pressed on and had produced an indentation in the optic nerves. In 11 cases the base of the brain was entirely free of arachnoidal adhesions. In the remaining 15 cases there was slight thickening of the arachnoid, which could be considered as still within the range of normal.

Advanced Age.—Optochiasmatic arachnoiditis has been said to be commonest between the ages of 20 and 40 years. Above the age of 50 it is rare. Nevertheless, brains of elderly persons were studied with the purpose of ascertaining whether a tendency to thickening of the arachnoid at the base of the brain is present in persons of advanced age. Thirty-seven brains of persons between 61 and 87 years of age were studied. There was no evidence that old age creates a predisposition to fibrosis of the arachnoid. In the oldest patient, aged 87, the interpeduncular space was entirely free of arachnoidal adhesions.

OTHER CAUSES

Among other diverse causes of optochiasmatic arachnoiditis, the French authors [1] mentioned frequent sore throat, erysipelas, furunculosis,

15. Bruetsch, W. L.: Rheumatic Endarteritis of Cerebral Vessels: Sequel of Rheumatic Fever, Tr. Am. Neurol. A. **68**:17, 1942.

16. Scheerer, R.: Netzhaut- und Sehnervenveränderungen bei Infektionskrankheiten, rheumatische Infektionen, Influenza und Grippe, Ergebn. d. allg. Path. u. path. Anat. (supp.) **21**:287 and 288, 1928.

typhus and acute enteritis. Unless an infection of the blood stream is associated with these conditions, setting up meningitis at the base of the brain, it is difficult from a pathologic point of view to see how optochiasmatic arachnoiditis could be produced. Infectious diseases, such as grip, influenza, mumps and scarlet fever, are mentioned as causes of arachnoiditis. In the older literature, cases with visual complications in the course of and following these diseases have been recorded, but they were interpreted at that time, and probably correctly, as the result of optic neuritis.[16] One should keep in mind that these conditions, particularly a scarlatinal infection, may produce widespread demyelination of the white matter.[17] The possibility of involvement of the visual fibers is always present in such demyelinating processes.

COMMENT

Except for the fact that syphilis is the most frequent cause of optochiasmatic arachnoiditis, occurring usually in asymptomatic form, the study has thrown little light on the etiology of optochiasmatic arachnoiditis. As in cases of arachnoiditis of the spinal cord,[18] in which it is often impossible to establish a definite etiologic factor, so it is impossible to determine the cause in a large number of cases of arachnoiditis of the optochiasmatic region.

It is true that trauma is a well recognized cause of arachnoiditis of the brain and spinal cord, particularly when the arachnoidal adhesions are located directly beneath a fracture of the skull or vertebrae. However, in cases of cerebral injury the exact mechanism of the development of optochiasmatic arachnoiditis, limited to such a narrow region as the optic chiasm, is obscure.

Davis and Haven,[19] who classified the histopathologic types of arachnoiditis as inflammatory, fibrotic and hyperplastic, made no attempt to discuss the etiologic factors in their cases, except in 1 in which trauma was the cause.

One fact, however, seems to emerge, namely, that the chiasmatic syndrome, which in most cases of optochiasmatic arachnoiditis has been attributed solely to the constricting effect of the arachnoidal adhesions, is due to a concomitant lesion within the chiasm or other parts of the visual pathways. This conclusion is illustrated by the case of Craig and Lillie,[4] in which a cystic area of degeneration was present in the optic chiasm. In patients with encephalitis, one can assume that the

17. Ferraro, A.: Allergic Brain Changes in Post-Scarlatinal Encephalitis, J. Neuropath. & Exper. Neurol. **3**:239, 1944.

18. Brouwer, B.: Ueber Arachnoiditis adhäsiva circumscripta, Deutsche Ztschr. f. Nervenh. **117**:38, 1931.

19. Davis, L., and Haven, H. A.: A Clinico-Pathologic Study of the Intracranial Arachnoid Membrane, J. Nerv. & Ment. Dis. **73**:129 and 286, 1931.

process may have also affected the optic chiasm and nerves, thus contributing to the visual complications.[20] In a number of cases which have been reported in recent years under the diagnosis of optochiasmatic arachnoiditis, the latter interpretation would have been more correct.

Cushing[2] has rightly pointed out that the answer to this question may lie in the fact that the same process which causes the thickening of the pia-arachnoid may affect, and permanently damage, the optic nerves. This, for instance, is true in some cases of syphilitic optochiasmatic arachnoiditis, in which the exudate at the base of the brain not only produces the thickening of the arachnoid, but also extends along the septums of the optic nerves, causing degeneration of the visual fibers.[21]

The mediocre operative results in a considerable number of cases in which the arachnoidal adhesions have been surgically removed seem to support such reasoning. The results so far as vision is concerned are far from being as favorable as those which follow removal of a tumor.[22] Of the largest series of cases in which operation was performed for optochiasmatic arachnoiditis, improvement occurred in 28 per cent, and the result of the operation was doubtful or poor in the remaining cases.

The atrophic effect of the arachnoiditis has been attributed to the constriction of the optic nerves by arachnoidal bands or to circumscribed collections of cerebrospinal fluid acting in the manner of a tumor. Anatomic experience, however, does not bear out the contention that direct local pressure or tension on the optic nerves and chiasm is an important factor in producing atrophy of the optic nerves. In cases of neoplasms of the pituitary body and other tumors at the base of the brain, the optic nerves and chiasm are at times reduced to ribbons by direct local pressure. Surprisingly, on microscopic examination, one will find a large number of intact nerve fibers, especially if the general intracranial pressure was only slightly elevated.

The problem of how much atrophy of the optic nerve is attributable to the mechanical constriction by the arachnoid is further complicated by the fact that a line of division between a normal and an abnormal arachnoid cannot be drawn with any precision. There are many cases with normal optic nerves and thickening of the optochiasmatic arachnoid which, in my opinion, is not outside the limits of physiologic variation, but which by neurosurgeons at the present time would be diagnosed as

20. Scheyhing, H.: Neuritis optica mit vorübergehender Erblindung und Meningo-Enzephalitis nach Schutzpockenimpfung, Klin. Monatsbl. f. Augenh. **102**: 223, 1939.

21. Bruetsch, W. L.: Malaria Therapy in Syphilitic Primary Optic Atrophy, J. A. M. A. **130**:14 (Jan. 5) 1946.

22. Hartmann, E.: Optochiasmic Arachnoiditis, Arch. Ophth. **33**:68 (Jan.) 1945.

optochiasmatic arachnoiditis. In such instances the slight arachnoidal thickening is merely incidental and may not be connected with the obscure atrophy of the optic nerve for which surgical intervention was attempted.

Judging from the recent literature, it is obvious that the tendency to report unexplained cases of optic nerve atrophy under the heading of optochiasmatic arachnoiditis is increasing.[23] Patients are known to have been operated on for optochiasmatic arachnoiditis who later proved to have multiple sclerosis. The clinical diagnosis of optochiasmatic arachnoiditis itself is unusually difficult because neither the visual fields nor the appearance of the optic disks is definitely characteristic of this condition. Hartmann [22] expressed the belief that there is at present no standard by which one can form a judgment before operation as to the cases in which surgical treatment will be of benefit and those in which the condition will not respond.

CONCLUSIONS

In a considerable number of cases of optochiasmatic arachnoiditis a definite etiologic factor cannot be established. The most frequent cause is syphilis. Another well recognized cause is otitis media, producing basilar arachnoiditis. The role of trauma in the production of isolated arachnoidal thickening in the optochiasmatic region is difficult to understand.

While arachnoidal adhesions alone may be responsible for atrophy of the superficial nerve fibers, anatomic experience tends to show that they do not produce atrophy of the optic nerves on a large scale.

In many cases reported under the designation of optochiasmatic arachnoiditis there is most likely a primary morbid process within the chiasm and optic nerves, either inflammatory or demyelinating, involving the nerve fibers and the arachnoid in variable proportions.

Lack of detailed microscopic studies of the chiasm and optic nerves in cases of optochiasmatic arachnoiditis makes impossible a complete evaluation of the problem at the present stage of knowledge.

Central State Hospital.

23. Ryan, E. R.: Optochiasmic Arachnoiditis: Report of Three Cases, Arch. Ophth. **29**:818 (May) 1943.

Case Reports

TRANSIENT HEMIPLEGIA FOLLOWING ELECTROCONVULSIVE TREATMENT

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ELECTROSHOCK therapy has proved its usefulness in the treatment of the major psychoses. Its value and its limitations are well established by everyday experience. However, there is still insufficient knowledge of the basic changes caused by electroshock therapy. Aside from the various psychologic theories, the simple question of what the current does to the brain structure has not yet been answered satisfactorily. Fatal incidents connected with this treatment, fortunately, are extremely rare, and only a small number of complications involving the central nervous system have been reported.

Olsen [1] described a case of unilateral convulsion and transient hemiplegia in a case of senile psychosis treated with electroshock. His case is to be distinguished from the average case of electroshock by so many features that it is difficult to draw generally applicable conclusions from his observation. Olsen's patient was 73 years of age and prior to the treatment had shown symptoms of cardiovascular disease of anginal character. The treatment was given after preparation with curare (intocostrin), and the hemiparesis lasted only half an hour.

In the case which is described here, complete hemiplegia occurred after electroshock in a young woman and lasted several days, gradually subsiding. The patient had not shown any cardiovascular disease, and neither curare nor any other drug was used.

REPORT OF CASE

A professional woman, aged 31, unmarried, was admitted to the Boston State Hospital on Nov. 22, 1944. For six months prior to her admission she had been under the treatment of a private psychiatrist for irritability and many vague somatic complaints. Two days before admission she became disturbed and tried to jump out of a window. After admission her talk and conduct were disorganized. At times she appeared depressed and voiced guilt feelings because she had not obeyed her parents. At other moments she was restless, overactive and even assaultive. After a few days of hydrotherapy she calmed down and was well behaved. She expressed self accusation concerning some sex play she had allowed herself with her "boy friend." Under psychotherapeutic treatment her condition continued to improve, but her family urgently requested her release from the hospital. On Jan. 27, 1945 she went home on a visit. In November 1945 she

From the Medical Staff of the Boston State Hospital.

1. Olsen, C. W.: An Unusual Reaction to Electroshock Treatment: Unilateral Convulsion and Transient Hemiplegia, Bull. Los Angeles Neurol. Soc. 9:171, 1944.

was returned to the hospital in a state of acute excitement, assaulted those about her and was profane in her language and hallucinated in the auditory field.

She received her first electroshock treatment on November 25. At that time she was greatly disturbed and resistive. Gradually she calmed down and after the seventh treatment was practically without gross mental abnormality. In order to maintain the result, treatment was continued at weekly intervals. On Feb. 7, 1946 she was given her tenth electroshock treatment. As with each previous shock, she had a general convulsion. No unusual observation was made at the time. Half an hour after the treatment she had recovered sufficiently to walk back to her ward. The following day she was less active than usual but was able to walk. No important change in her condition was noticed by the ward personnel or by the physician on his rounds. However, during the night of February 8 she was restless, and the next morning she was unable to get up. When trying to leave her bed, she slipped to the floor and had to be helped back to bed by an attendant.

Neurologic examination made early on the morning of February 9 showed that she was conscious and in fairly good contact, but tense and at times unwilling to cooperate. She seemed to be frightened by her physical condition, did not talk and produced moaning sounds. Her left arm and hand were limp and totally paralyzed; her left leg was weak and partially paralyzed. No difference in the facial innervation of the two sides could be seen. The tongue deviated to the left but could be moved to either side. The pupils reacted to light and in accommodation and were equal. All tendon reflexes were hyperactive on the left side. There were definite Hoffmann and Oppenheim signs on the left; the Babinski sign was equivocal. The eyegrounds were normal.

Examination on February 11 showed pronounced improvement in the motor power of the left leg. She was still unable to move the arm, but slight movements of the hand were possible. The tendon reflexes were still hyperactive on the left side, and the Hoffmann and Oppenheim signs could be elicited. The patient was much calmer, was able to say a few words and showed better cooperation.

On each of the following days the condition continued to show improvement. On February 14 she was able to walk, and on February 15 the paralysis had completely disappeared. There was still slight hyperactivity of the tendon reflexes of the left side, but the Oppenheim and Hoffmann signs could not be elicited. The patient had a slight subjective feeling of weakness in the left leg on walking. These symptoms subsided during the following days and did not recur. The latest neurologic examination, made in March 1947, more than a year after the incident, revealed nothing abnormal.[2]

The patient's mental improvement was not sustained. A few weeks after termination of the shock treatment she relapsed into her previous mental condition. The experience of her hemiplegia has now been included in her paranoid ideation. She thinks that she was used for the purpose of experimentation, and she refused to submit to further electric treatment. This idea caused the failure of many attempts to perform an electroencephalographic examination. She objected emphatically, and when, after much persuasion, the electrodes were applied she pulled them off. The attempts were repeated, and finally, on March 3, 1947, an electroencephalogram was obtained.[3]

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2. The patient was seen in consultation with Dr. Elvin V. Semrad, clinical director, Boston State Hospital, who confirmed the neurologic findings.

3. Dr. Rudolph Neustadt interpreted the electroencephalogram.

This record was characterized by regular and irregular activity, with a frequency of 8 to 10.5 cycles per second and an amplitude of 50 to 55 microvolts. The average activity had a frequency of 8.5 cycles per second and an amplitude of 50 microvolts. Hyperventilation was not carried out, as the patient was not sufficiently cooperative. No signs of localization were present. The record was classified as normal.

This electroencephalographic pattern is in accordance with the neurologic findings at the time of this report. The pathologic signs disappeared when the hemiparesis subsided, and during an observation of more than a year no residual signs of any focal lesion of the brain have been noted.

COMMENT

In patients with spontaneous epileptic seizures the question of vascular spasm has long been studied. Kennedy [4] described pallor of the brain on the operating table preceding a convulsion. Other authors observed preconvulsive vasoconstriction but doubted the importance of this phenomenon in the pathogenesis of the seizure. Milch [5] studied the retinal arteries before and after shock in patients receiving electroshock treatment. He found spasm of the retinal arteries usually preceding the generalized convulsion. Alexander and Loewenbach [6] in animal experiments observed that arteriolar vasoconstriction and blanching were noticeable within the path of the current for less than half an hour. Only doses far beyond those used in clinical practice produced vasoparalytic stasis.

All these observations indicate that vasomotor phenomena are connected with electrically induced convulsions. The transient hemiplegia in our case might best be explained on the basis of a vascular spasm, leading to reversible damage in the motor system of the brain. The arteriolar constriction must have lasted long enough to cause structural damage. It took more than thirty-six hours before this damage was sufficiently severe to produce noticeable symptoms. The pathologic condition must have occurred in the motor pathways of the right hemisphere, most probably in the internal capsule, where even slight lesions produce clear evidence of dysfunction.

CONCLUSIONS

The investigations of Kennedy [4] showed arterial spasm during spontaneous epilepsy. Milch's studies of the eyegrounds, the animal experiments of Alexander and Loewenbach and the observation in this case seem to justify the assumption that cerebral vasoconstriction generally occurs during electroshock treatments. Only because the vascular spasm occurred within the motor pathways did it produce the alarming and easily detectable symptoms which appeared in this unique case.

4. Kennedy, F.: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567 (May) 1923.

5. Milch, E. C.: Changes in Retinal Arteries Before Convulsions Induced by Electric Shock, Arch. Neurol. & Psychiat. **45**:848 (May) 1941.

6. Alexander, L., and Loewenbach, H.: Experimental Studies in Electroshock Therapy, J. Neuropath. & Exper. Neurol. **3**:139, 1944.

SUMMARY

A case of transient hemiplegia of several days' duration following electroconvulsive treatment was observed in a physically normal young woman with a schizoaffective psychosis. Only 1 somewhat similar case has been reported (Olsen.[1]) However, Olsen's case was essentially different, as the patient had severe vascular disease, was old and had received curare and his hemiplegia had lasted only a half-hour. No other observation of this kind was found in the literature.

An explanation of the pathologic process is offered on the basis of vascular spasm, which causes structural damage in the motor pathways of one side of the brain. Experimental investigations and clinical observations of cerebral vasoconstrictions in the course of electroshock therapy are discussed.

The present observation is reported as a contribution to an understanding of the neuropathologic lesions occurring with electrically induced convulsions.

Boston State Hospital (24).

POSTVACCINAL (TYPHOID) ENCEPHALITIS

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IN RECENT years instances of acute disseminated encephalitis are being recognized with progressively increasing frequency. This increase probably represents a true rise in the incidence of such disease, not merely an apparent rise. For many years the term "encephalitis" was used to refer specifically to viral or bacterial diseases or to conditions suspected of having such an origin. Recently, it is becoming increasingly apparent that many, if not the majority of, encephalitides are noninfectious in origin and that they may well represent the acute stages of conditions previously considered degenerative. For the sake of clarity, it is well to consider three types of disseminated encephalitis, namely, the infectious, the definitely noninfectious and the diffuse demyelinating diseases of questionable origin. Many authors have attempted to subclassify the last type, the so-called acute demyelinating diseases, but this endeavor is made difficult by the frequent coexistence of lesions in the gray and the white matter and by the inexact methods of defining damage inflicted on cells and axis-cylinders. For simplification, it is well to classify as demyelinating diseases any pathologic process in which the lesions are predominantly in the white matter, leaving the gray matter relatively unaffected.

Demyelination may represent simply a part of a general necrosis which includes all structures within a certain area; it may be a retrograde degenerative phenomenon, or it may, apparently, represent the primary response of the nervous system to the disease process. In the infectious encephalitides, demyelination is simply one of many pathologic changes, which also include lymphocytic infiltration and often demonstrable inclusion bodies; the infectious group is relatively well understood, and at least stands with the conditions in which there is a demonstrable and viable etiologic agent. Among the definitely noninfectious encephalitides, more particularly those of the deficiency diseases and the heavy metal poisonings, demyelination often forms the sole demonstrable pathologic change; here, however, the pathologist's conscience is relieved by the demonstration of chemically measurable toxic factors or of a

From the Section of Neuropathology (Dr. Kernohan).

definite lack of essential factors. The third type—disseminated demyelinating diseases—overlaps the second type and at present includes a number of the misunderstood encephalitides. It is our belief that any case which sheds light on the etiologic factor in such disease processes is worthy of careful investigation; for that reason, we feel justified in reporting a case, in which the patient was recently seen by one of us (H. M. R.).

REPORT OF CASE

A white woman aged 21, when first examined, on Nov. 28, 1945, complained chiefly of nausea, malaise and mental confusion, accompanied by weakness of the left arm, the left leg and the left side of the face. For two and a half years the patient had been employed as an undergraduate nurse. Two days prior to examination the patient had received 0.5 cc. of typhoid vaccine U. S. P. subcutaneously for purposes of immunization, as required by the nursing school. This was followed on the same day by some degree of listlessness. The next day there were nausea and one episode of vomiting, but she had continued to work, stopping at approximately 11 p. m. On the day of her admission she felt weak but reported for work at 4 p. m. The other nurses noted that she acted strangely, and during the evening it became apparent that the left side of her face was becoming drawn.

The history of the patient was noncontributory except for an injury to the right eye, sustained six years previously. This had resulted in retinal detachment and a traumatic cataract. There was no history of allergic manifestations. In July 1943 she had been immunized with three inoculations against typhoid. In March 1944 she had been hospitalized for one week because of unexplained nausea and vomiting.

Physical examination at the time of the patient's admission revealed a temperature of 98.4 F. (36.8 C.), a pulse rate of 80 beats per minute and a respiratory rate of 20 per minute. The blood pressure was 110 mm. of mercury systolic and 80 mm. of mercury diastolic. She appeared listless, and her speech was thick and slurred. There was a traumatic cataract of the right eye; the left optic disk had an indistinct nasal margin. Ocular motions were normal with the exception of limitation on left lateral gaze. The tongue deviated to the left, and there was definite weakness of moderate degree in the left arm and leg, with a Babinski reflex (great toe) on that side. The heart, lungs and abdomen were normal.

Essential laboratory studies revealed the hemoglobin content to be 15.6 Gm. per hundred cubic centimeters of blood. The erythrocytes numbered 4,700,000 and the leukocytes 8,850 per cubic millimeter of blood, with a normal differential count. The reaction to the Kahn test was negative. The clot retraction, bleeding time and coagulation time were normal. The cerebrospinal fluid was clear and under a pressure of 180 mm. of water, with 1 cell per cubic millimeter of fluid and a total protein content of 18 mg. per hundred cubic centimeters of fluid; the colloidal gold curve was normal and the reaction to the Kahn test was negative; the value for sugar was 54 mg. per hundred cubic centimeters of fluid. Spinal puncture was repeated in ten days, and similar observations were made. Roentgenograms of the thorax and skull showed no abnormalities.

During the first twenty-four hours complete paralysis of the left extremities developed, associated with slight paralysis of the left side of the face. The patient remained rational for approximately one week, but she was listless and speech was thick. Numbness of the left arm became troublesome, but the sensorium and

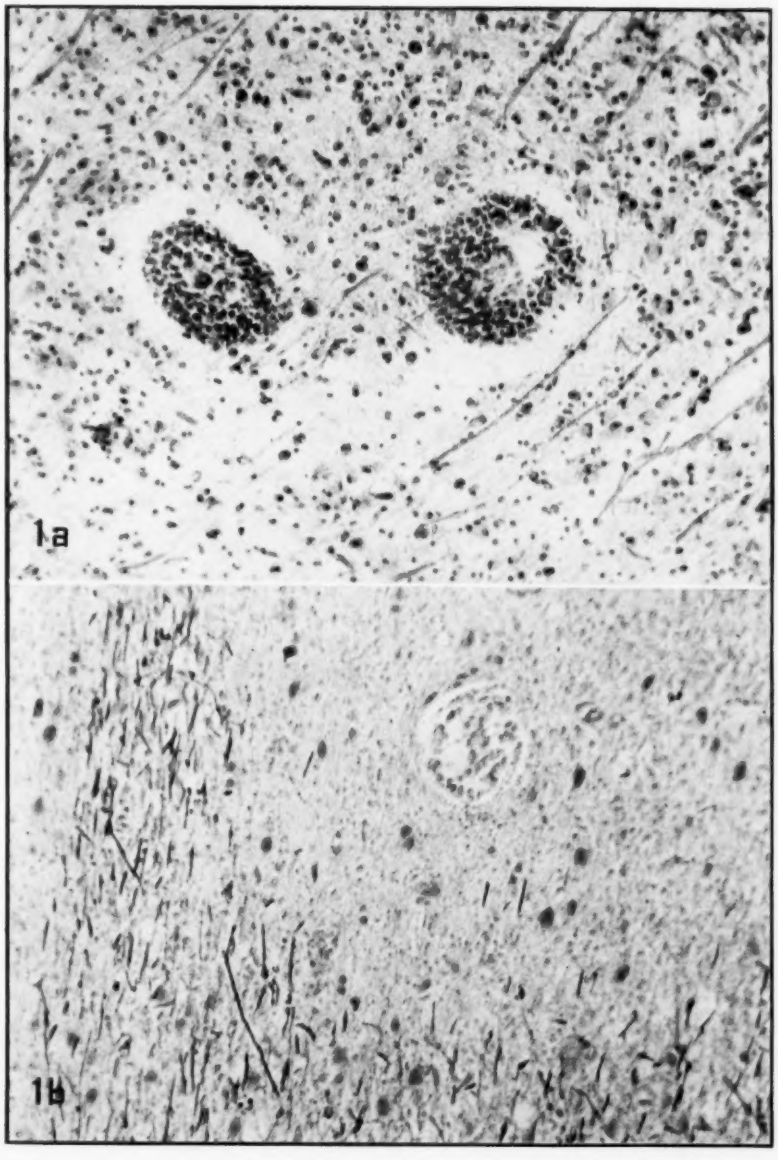

Fig. 1.—(*a*) Section from the cortex of the right occipital area, showing scattered phagocytes containing neutral fat, the end stage in the breakdown of myelin (scarlet red–frozen fat technic; × 85). (*b*) Section from the cortex of the right frontal area, showing perivascular phagocytic proliferation, with surrounding edema and loss of brain substance. The periphery of this photograph exhibits a transition zone, with evidence of disorganization, but relatively intact myelin sheaths (Weigert stain; × 85).

mental attitude remained normal. With the exception of an increase in temperature to 99.2 F. (37.3 C.) on the third to the fifth day of her illness, she remained afebrile until the terminal stage.

At the end of a week, the patient appeared less listless and her speech improved, but the paralysis remained unchanged. There was complete left hemiplegia, including the face, tongue and palate. The deep reflexes were hyperactive on the left side, with a corresponding Hoffmann sign and Babinski reflex. The abdominal reflexes were absent on the left side but active on the right. Funduscopic examination revealed nothing pathologic, but gross homonymous hemianopsia, probably complete, was present on the left. No evidence of meningeal irritation developed.

The condition of the patient remained stationary except for slight improvement in her speech. On December 25 she was permitted to sit out of bed for five minutes. That evening it was noted that she had lost her speech and that she seemed extremely depressed; periods of crying alternated with episodes of childish laughter. Two days later, she became semistuporous, and her temperature increased to 99.3 F. (37.4 C.). The stupor progressed and was accompanied with an increase in temperature, which reached 107 F. (41.7 C.) terminally. There was a corresponding increase in pulse rate. On the twenty-eighth day intermittent convulsions developed, associated with hyperventilation. The coma progressed, and the patient died of respiratory failure at 4:30 p. m., December 29 (thirty-two days after the onset of illness).

Necropsy was performed approximately two hours after the patient's death, the body having previously been embalmed with solution of formaldehyde U. S. P. The pertinent gross anatomic observations were limited to the brain, which was intensely congested and edematous. In the right parieto-occipital region was an area, approximately 5 by 4 by 4 cm., which was soft and grayish white. The gross changes were entirely within the white matter; the gray matter appeared to be essentially normal. A similar area of softening was noted in the right frontal region, separated from the former lesion by a portion of normal-appearing brain. There was no evidence of meningitis or hemorrhage. The vessels were carefully examined for occlusion or atheromatous plaques, but none could be found.

Gross examination of the organs of the thorax and abdomen revealed no abnormality.

All major portions of the brain were sectioned for microscopic study. Special staining methods included the Weigert, Bodian activated silver, cresyl violet, Mallory phosphotungstic acid hematoxylin, Mallory-Heidenhain and scarlet red-frozen fat technics.

Microscopically, all portions exhibited some pathologic change, varying from moderate oligodendroglial proliferation, in the basofrontal regions, to almost complete and widespread demyelination, in the right occipital lobe. In the two areas most severely involved, namely, the right occipital and the right anterior frontal (figs. 1 and 2), the most striking changes were the perivascular collections of large, fat-laden phagocytes (figs. 1*a* and 2*a*) and the spotty demyelination (figs. 1*b* and 2*b*). In many areas the myelin immediately surrounding large vessels was relatively intact, in spite of the presence of marked phagocytic proliferation in the adventitia. In the right occipital area, where demyelination was most complete and the process relatively old, the axis-cylinders had almost completely disappeared, whereas in the right frontal area they were in part preserved; these facts suggest that damage to myelin and damage to axis-cylinders often coexist, the latter following, but being associated with, the former. In all sections the glial fibers were well preserved, as were the nerve cells in the cortex. Where

the pathologic process was active, the astrocytes were greatly swollen, and in some regions of the *gemästete* type; but there was no actual proliferation of astrocytes. The brain as a whole was edematous, with separation of brain substance and enlargement of the Virchow-Robin spaces. Careful search for thrombi revealed no evidence of occlusion. In many areas there was proliferation of the endothelial cells of the smaller blood vessels, but no true thrombi were present.

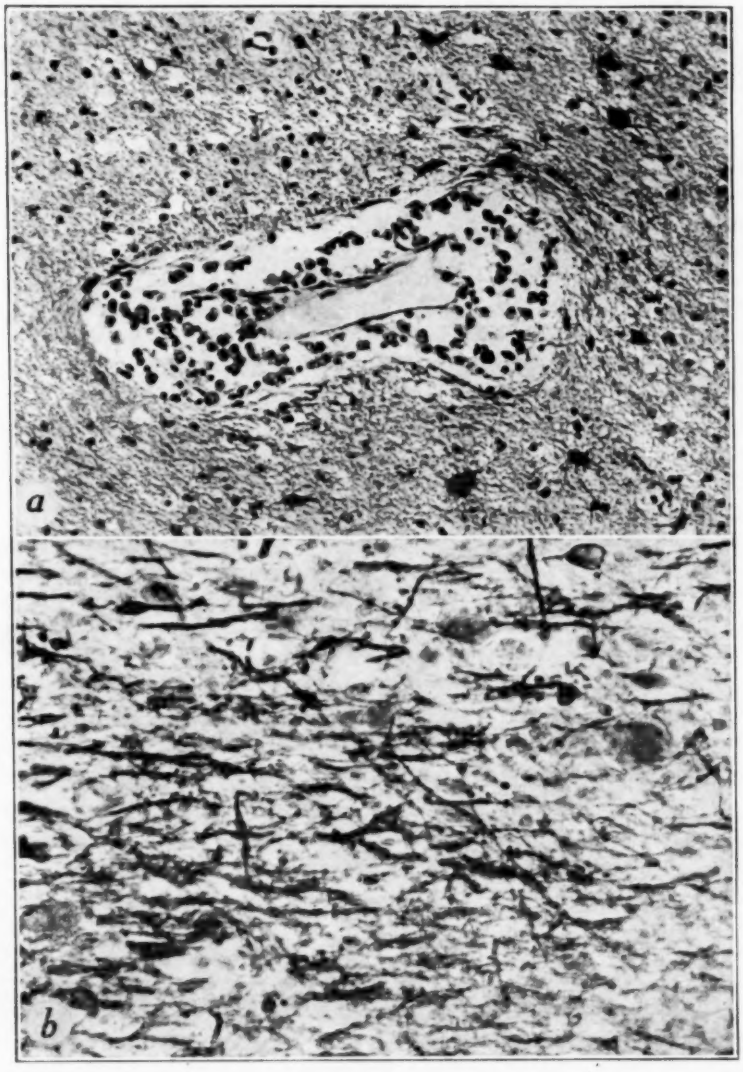

Fig. 2.—(*a*) Section from the right occipital area, showing enlargement of the Virchow-Robin spaces, with proliferating lipophages, and also representative absence of the perivascular cuffing seen in virus encephalitides (hematoxylin and eosin stain; × 175). (*b*) Section from the cortex in the right frontal area, showing a portion of partial demyelination, with fragmented, swollen and bulbous myelin sheaths; many swollen astrocytes and lipophages are seen between degenerating myelin sheaths (Weigert stain; × 235).

The cortex was relatively normal in appearance except for an oligodendroglial increase in its lower layer. The cerebellum, midbrain, pons and medulla were essentially normal.

COMMENT

Many cases of postvaccinal encephalomyelitis and several cases of postrabietic encephalomyelitis have been reported, but only a few in which the condition followed inoculation with typhoid have been recorded. Because such cases may lend additional weight to the theory of the allergic basis of the condition, it seems well to evaluate the etiologic factors in the present case. Since the introduction of inoculation against typhoid, in 1896, the procedure has been carried out millions of times, and the incidence of even minimal toxic reactions has been astoundingly low. For many years it has been recognized that inoculation against typhoid may activate latent chronic infections, especially tuberculosis, but few lesions of the central nervous system have been reported.

The earliest reported instances of the condition in question apparently are those of Gubb,[1] who in 1915 described several cases in which neurologic symptoms followed inoculation against typhoid. Three years later, Roussy and Cornil[2] described 2 cases in which the symptoms were suggestive of cortical thrombosis, but in which recovery ensued. The first reported instance of death was that of Guillain and Barré,[3] who described a case in which ascending myelitis developed, followed by death nine days after the fourth injection, of 1.5 cc., of typhoid and paratyphoid vaccine. Since that time, Léri and Boivin[4]; Preti[5]; Souques[6]; Bury[7]; Gayle and Bowen[8]; Russell[9]; Alajouanine,

1. Gubb, A. S.: Case of Nervous Disturbances After Anti-Typhoid Vaccination, M. Press **100**:371, 1915.

2. Roussy, G., and Cornil, L.: Monoplégie brachiale sensitive avec ataxie, léger tremblement et attitudes athétosiques consécutive à des injections de vaccin antityphique, Rev. neurol. **26**:453-456, 1919.

3. Guillain, G., and Barré, J. A.: Paralysie ascendante aiguë de Landry consécutive à une vaccination antityphoïdique, Rev. neurol. **26**:595-598, 1919.

4. Léri, A., and Boivin: Un cas de paralysie ascendante aiguë de Landry après une vaccination antityphique (T. A. B.); guérison, Rev. neurol. **26**:965-967, 1919.

5. Preti, L.: Stati morbosi susseguenti alla vaccinazione tifoidea, Atti d. Soc. lomb. di sc. med. e biol. **8**:85-89, 1919.

6. Souques, M. A.: Syndromes nerveux consécutifs à la méningite antityphoïdique, Rev. neurol. **26**:501-505, 1919.

7. Bury, J. S.: Symptoms Resembling Tabes Dorsalis, Arising After Anti-typhoid Inoculation, Lancet **2**:844-845 (Oct. 23) 1920.

8. Gayle, R. F., Jr., and Bowen, R. A.: Acute Ascending Myelitis Following the Administration of Typhoid Vaccine: Report of a Case with Necropsy Findings, J. Nerv. & Ment. Dis. **78**:221-231 (Sept.) 1933.

9. Russell, J. L.: Report of Two Deaths from Third Inoculation with Typhoid Para-Typhoid Vaccine: Some Observations on Typhoid Inoculation, Kentucky M. J. **22**:378-382 (Oct.) 1924.

Fribourg-Blanc and Gauthier [10]; Kennedy [11]; Noica [12]; Robinson,[13] and Peacher and Robertson [14] have reported a total of 16 cases in which complications occurred; it is interesting that the majority of the patients presented symptoms referable to the spinal cord. Of these cases, only that of Peacher and Robertson [14] was given an adequate pathologic study.

The question of the etiologic factor in such cases remains unsettled. The theory of the infectious nature of the condition has been reasonably well disproved, both by virtue of the negative results of virus and bacteriologic studies and by the dissimilarity of the pathologic changes in cases of these encephalitides to those which occur with the definitely infectious encephalitides. As Rivers [15] stated, "no known virus acting directly on the central nervous system produces a perivascular demyelinating type of encephalitis." Cerebral injection of viruses of rabies and vaccinia never produces a demyelinating reaction; yet encephalitis which follows such inoculation is characterized by perivascular demyelination. The role of various toxic factors always remains a distinct possibility; that such factors can produce demyelinating disease processes has been well shown in the case of poisoning with lead and other heavy metals, as well as in the case of poisoning with such substances as triorthocresyl phosphate.[16] Weil and Heilbrunn's [17] demonstration of the presence, in patients who have multiple sclerosis, of a myelolytic substance which is excreted in the urine raises the entire problem of the production by the body of intermittently active chemical substances, such as that seen with recurrent porphyria. The toxic basis of a condition such as the one we have reported cannot be ruled out, but it seems unlikely.

The most challenging theory as to the etiologic basis of a majority of the demyelinating diseases, particularly those designated as "idio-

10. Alajouanine, T.; Fribourg-Blanc, A., and Gauthier: Un cas de poliomyélite antérieure consécutive à une vaccination antityphoïdique, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:446-450 (March 15) 1928.

11. Kennedy, F.: Certain Nervous Complications Following the Use of Therapeutic and Prophylactic Sera, Am. J. M. Sc. **177**:555-559 (April) 1929.

12. Noïca, D.: Trois cas d'accidents à la suite d'injections de vaccin typho-paratyphique, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:1026-1028 (June 27) 1932.

13. Robinson, L. J.: Neurologic Complications Following the Administration of Vaccines and Serums: Report of a Case of Peripheral Paralysis Following the Injection of Typhoid Vaccine, New England J. Med. **216**:831-837 (May 13) 1937.

14. Peacher, W. G., and Robertson, R. L.: Neurological Complications Following the Use of Typhoid Vaccine, J. Nerv. & Ment. Dis. **101**:515-526 (June) 1945.

15. Rivers, T. M., in Round Table Discussion on Encephalitis, J. Pediat. **8**:518-521 (April) 1936.

16. Smith, M. I.; Elvove, E., and Frazier, W. H.: The Pharmacological Action of Certain Phenol Esters, with Special Reference to the Etiology of So-Called Ginger Paralysis, Pub. Health Rep. **45**:2509-2524 (Oct. 17) 1930.

17. Weil, A., and Heilbrunn, G.: Demonstration of Myelolytic Substances in Disseminated Sclerosis, Proc. Soc. Exper. Biol. & Med. **48**:233 (Oct.) 1941.

pathic," is that of the hypersensitivity or allergic condition of the individual patient. Allergy of the central nervous system is a definitely observed entity, as neatly portrayed by Clarke.[18] As he pointed out, a sensitized tissue responds to its specific protein with the production of local edema, spasm of smooth muscle and hyperactivity of glandular secretion. When such reactions occur in the central nervous system, the edema is the prominent anatomic feature, and localized or generalized signs of increased intracranial pressure may well develop. Kennedy [11] has given typical instances of transient symptoms referable to the central nervous system occurring after the use of therapeutic and prophylactic serums; he suggested that such reactions probably have a basis in some type of angioneurotic edema. It is possible that in many cases the as yet unexplained increased intracranial pressure has a similar cause. The relation of such a response to cyclic psychic phenomena can be merely suggested. Urticarial-like sensitivity, however, does not explain demyelination; a more truly anaphylactic reaction might do so. Jervis, Ferraro and associates [19] produced a typical Arthus phenomenon with the intracerebral injection of antigen. The local lesions were characterized by edema, destruction of tissue, hemorrhage and infiltration of polymorphonuclear cells. Similar results had been produced previously in guinea pigs by Davidoff.[20] The important observation in both experiments was not establishment of the Arthus phenomenon but demonstration of associated demyelination of portions of the remaining part of the brain.

With such facts in mind, it is well to recall that postvaccinal encephalitis occurs with great regularity at a time when immunity is at its height and revaccination is impossible. This has been demonstrated conclusively in the case of vaccinia, in which the reaction usually occurs on the eleventh day after the inoculation; and it will probably also prove to be true for the reactions to inoculation for typhoid; as yet not enough cases have been reported for us to be certain of this occurrence. In the case we have reported, however, the disease followed the usual trend of occurring in a previously inoculated person who was undergoing reinoculation. It is also well to recall that in inoculation against typhoid, dead or attenuated bacteria are injected, and that these constitute an optimal source of foreign protein.

Such experimental and clinical observations seem to hint, at least, at a possible solution of a poorly understood and often ignored group of neurologic disturbances. Whether the answer will lie in an anaphylactic reaction which affects the coagulability of blood, as described by Putnam,[21] whether it will reside in a histamine-like substance liberated

18. Clarke, T. W.: Allergy of Central Nervous System, Ann. Allergy **2:** 189-196 (May-June) 1944.

19. Jervis, G. A.; Ferraro, A.; Kopeloff, L., and Kopeloff, N.: Neuropathologic Changes Associated with Experimental Anaphylaxis in the Monkey, Arch. Neurol. & Psychiat. **45:**733-751 (May) 1941.

20. Davidoff, L. M.; Siegal, B., and Siegal, D.: The Arthus Phenomenon: Local Anaphylactic Inflammation in the Rabbit Brain, J. Exper. Med. **55:**163-168 (Jan.) 1932.

21. Putnam, T. J.: Newer Conceptions of Postinfectious and Related Forms of Encephalitis, Bull. New York Acad. Med. **17:**337-347 (May) 1941.

in the brain or whether it will be found to be an altogether unexpected substance is a problem for the future. Cases such as the present one merely point the way for investigation.

SUMMARY

A case in which localizing symptoms in the central nervous system developed in a young woman after inoculation against typhoid is reported. Pathologic changes included widespread demyelination and proliferation of lipophages, without evidence of infection. The possible relation of the condition to an allergic reaction is suggested.

The Mayo Clinic.

News and Comment

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY

The next annual meeting of the American Association on Mental Deficiency will be held in Boston, at the Copley Plaza, May 18 to 22, 1948, instead of at the Hotel Statler the previous week. This meeting is to commemorate the one-hundredth anniversary of the first school for mentally defective persons in the United States. It will be the first international congress on mental deficiency ever held.

INTERNATIONAL CONFERENCE ON PSYCHOSURGERY

The date set for the International Conference on Psychosurgery, to be held in Lisbon, Portugal, has been changed to the first week of August 1948.

This change has been made to give those who wish to attend the International Congress on Mental Health, to be held in London later in August, an opportunity to do so without loss of time.

ANNOUNCEMENT OF FELLOWSHIPS IN CHILD PSYCHIATRY

The American Association of Psychiatric Clinics for Children offers fellowships for training in child guidance clinic psychiatry under the auspices of the United States Public Health Service, The Commonwealth Fund and some local funds. The training is for positions in community clinics where psychiatrists, psychologists, social workers and others collaborate in the treatment of children with emotional or mental illness.

Most of the fellowships are for two years; some, for one. The stipend is $3,000 for the first year, and more for the second. Prerequisites are graduation from an approved medical school, a general internship and two years of general psychiatry.

Opportunity is provided for the fellow to develop his own skills in a well organized outpatient service with the support of a carefully planned training program and adequate supervision. The training centers are selected on the basis of standards which have been established by the American Association of Psychiatric Clinics for Children, and the fellowships are awarded by a committee of this organization.

For further information, write Dr. A. Z. Barhash, executive assistant, The American Association of Psychiatric Clinics for Children, 1790 Broadway, New York 19.

Resignation of Dr. Nathan Blackman as Chief Psychiatrist, Mental Hygiene Clinic

Dr. Nathan Blackman announces his resignation as chief psychiatrist, Mental Hygiene Clinic, Veterans Administration Facility, St. Louis. In association with Dr. Louis L. Tureen, he will open a neuropsychiatric clinic at 440 North Taylor Avenue, St. Louis.

CORRECTION

In the article entitled "Electroencephalographic Studies on Induced and Excised Epileptogenic Foci in Monkeys," by Bernard L. Pacella, M.D.; Lenore M. Kopeloff, Ph.D., and Nicholas Kopeloff, Ph.D., which was published in the December 1947 issue of the ARCHIVES, the column heads "Seizures" in the upper half of table 1, page 694, should read "Seizures Opposite," as in the lower half of the table.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

REGULATION OF PITUITARY ADRENOCORTICOTROPHIC ACTIVITY DURING THE RESPONSE OF THE RAT TO ACUTE STRESS. G. SAYERS and M. A. SAYERS, Endocrinology **40**:265 (April) 1947.

Sayers and Sayers studied the action of acute stress in modifying the elaboration of adrenocorticotrophic hormone by the anterior lobe of the pituitary gland. The changes in adrenocorticotrophic activity of the pituitary gland occurring within one hour or less after exposure of an animal to any one of a number of stresses (cold, heat, injection of histamine, epinephrine or killed typhoid organisms) were measured by the alterations in the ascorbic acid content of the adrenal gland. Exposure to such stresses for one hour brings about a reduction in the concentration of ascorbic acid in the adrenal gland of the rat. The reduction in ascorbic acid content indicates stimulation of the anterior lobe of the pituitary to elaborate adrenocorticotrophic hormone. If a preparation of adrenal cortex hormone is administered prior to the application of stress, no reduction in the concentration of ascorbic acid in the adrenal glands takes place. Hence, the administration of cortical hormone acts to inhibit the increase in activity of the adrenal cortex which normally follows application of noxious stimuli. The degree of inhibition of adrenocorticotrophic activity of the anterior lobe of the pituitary gland is proportional to the amount of administered cortical hormone. The greater the degree of stress to which the animal is subjected, the greater the amount of cortical hormone required to inhibit adrenocorticotrophic activity.

The authors believe that stresses increase the adrenocorticotrophic activity of the pituitary gland by increasing the requirement of the peripheral tissue cells for cortical hormone. The anterior lobe of the pituitary responds to decreased concentration of cortical hormone in body fluids by increasing the rate of elaboration of adrenocorticotrophic hormone.

Since pituitary-inhibitory potency resides in compounds which are qualitatively distinct from each other in their metabolic activity—i. e., 17-hydroxycorticosterone, 17-hydroxy-11-dehydrocorticosterone, corticosterone, desoxycorticosterone and progesterone—the authors hypothesize that the steroids act directly on the anterior lobe of the pituitary rather than indirectly, through some product of their metabolic activity or through their deficiency.

FRANKEL, Philadelphia.

THE EFFECT OF GROWTH ON THE LIPID COMPOSITION OF RAT TISSUES. H. H. WILLIAMS, H. GALBRAITH, M. KAUCHER, E. Z. MOVER, A. J. RICHARDS and I. G. MACY, J. Biol. Chem. **161**:475, 1945.

The lipid distribution—phospholipid (cephalin, lecithin and sphingomyelin), free and combined cholesterol, cerebrosides and neutral fat—has been determined in tissues (brain, heart, kidney, lung, testis, liver, thymus, spleen and skeletal muscle) of rats 15, 45 and 70 days old. All the tissues increase in essential lipid content during growth. This increase is a reflection of the phospholipid, which is the

major component of the essential lipids. The other components of the essential lipid, cerebrosides and cholesterol, vary independently, not only with respect to each other but also with respect to the total, during growth of the rat between the ages of 15 and 70 days. The fundamental change, quantitatively, in lipid composition during growth, common to all the tissues studied, appears to be an increase in cephalin concentration. Specific changes in the various organs during growth are an increase in cerebrosides in testis and skeletal muscle and a decrease in cardiac muscle; a decrease in free cholesterol and sphingomyelin in both skeletal and cardiac muscle, and an increase in sphingomyelin in kidney, lung and spleen. All essential lipid components except lecithin and cholesterol esters show a considerable increase in the brain during growth. The probable relation of these changes in lipid composition and pattern among the various tissues to the structural and functional growth of the tissue are discussed.

PAGE, Cleveland.

EFFECTS OF LOWERING THE BLOOD p_H ON EXCITABILITY OF THE NERVOUS SYSTEM. HAROLD KOENIG and RICHARD A. GROAT, J. Neurophysiol. **8**:267 (July) 1945.

Koenig and Groat studied cats under anesthesia induced with chloralosane (a preparation of chloral hydrate and dextrose) and observed the alterations in responses to electrical stimulations administered to various parts of the peripheral and the central nervous system when the p_H of the blood was altered by means of intravenous injection of dilute hydrochloric acid or a sodium lactate buffer. The greatest reductions in excitability occurred in reflex arcs. During reductions in p_H of the blood the changes in excitability of supranuclear centers were of much smaller magnitude, but were considerable. Motor nuclei and peripheral motor nerves underwent the least reduction in excitability.

FORSTER, Philadelphia.

PROPERTIES OF MAXIMAL SEIZURES AND THEIR ALTERATION BY ANTICONVULSANT DRUGS AND OTHER AGENTS. JAMES E. P. TOMAN, EWART A. SWINYARD and LOUIS S. GOODMAN, J. Neurophysiol. **9**:231 (May) 1946.

The authors produced seizures in rabbits, cats and rats. Varying intensities of electroshock were employed, and it was found that seizures produced by shocking currents not far above threshold were usually of extreme tonic extensor type and were relatively constant in duration. Additional stimulation failed to modify the seizure once it had begun. When the tonic extensor component was abolished by repeated electroshock, it could be restored by stimulation during a seizure. The depression following tonic extensor convulsions was uniform in duration and greater than the depression following purely clonic convulsions. The authors conclude that the tonic extensor seizure represents the maximal rate of dissipation of energy of which the brain is capable.

The clinically recognized antiepileptic agents abolished the tonic phase of major seizures even when these drugs failed to raise appreciably the threshold for electroshock or metrazol seizures. The highest protective index was shown by diphenylhydantoin and phenobarbital. Pentobarbital was less efficient, and several new preparations, including "tridione" (trimethadione N. N. R.), ranked with pentobarbital.

The authors suggest use of the supramaximal electroshock method for laboratory identification and assay of antiepileptic drugs but feel that it should be used as a supplement to other technics.

FORSTER, Philadelphia.

EFFECT OF DI-ISOPROPYL FLUORPHOSPHATE (DFP) ON ACTION POTENTIAL AND CHOLINE ESTERASE OF NERVE. T. H. BULLOCK, H. GRUNDFEST, D. NACHMANSOHN, M. A. ROTHENBERG and K. STERLING, J. Neurophysiol. **9**:253 (May) 1946.

Bullock, Grundfest, Nachmansohn, Rothenberg and Sterling employed diisopropyl fluorophosphate in studies on the role of acetylcholine in the transmission of nerve impulses. Diisopropyl fluorophosphate is a new drug, which has an irreversible anticholinesterase activity. Transmission of nerve impulses in squid nerve and in the abdominal nerve chain of lobsters was studied, and the effects of diisopropyl fluorophosphate on this transmission were observed. Abolition of the action potential was found; this abolition was at first reversible if the nerves were washed in sea water. Longer maintenance of the nerve in solutions of diisopropyl fluorophosphate resulted in increasingly incomplete reversibility. The degree of reversibility of the action potential was found to parallel the amount of cholinesterase which reappeared in the nerve preparation. The authors conclude that inhibition of cholinesterase by diisopropyl fluorophosphate in the nerves of cold-blooded animals is partly reversible for a certain period. The observations are consistent with the concept that release and rapid removal of acetylcholine is an essential event during conduction.

FORSTER, Philadelphia.

GUIDES FOR NERVE REGENERATION ACROSS GAPS. PAUL WEISS and A. CECIL TAYLOR, J. Neurosurg. **3**:375 (Sept.) 1946.

Weiss and Taylor report the results of their animal experiments on the regeneration of nerves across gaps too extensive for primary end to end anastomosis. Gaps as great as thirty times the diameter of the severed nerves were bridged with use of arterial sleeves or collagen tubes, filled with a blood core. In one series, large numbers of leukocytes were added to the core to increase the liquefaction of the blood. Regeneration of fibers was excellent so long as the tubes remained patent. The longer the tube used, the greater was the degree of collapse. To avoid this, fiber cores of glass wool, nylon, textile rayon, cellulose acetate and "cordura" (tire rayon) were added to the sleeves or tubes. As long as these cores were in direct contact with the regenerating nerve, growth progressed. The fibers were then attached to both the proximal and the distal nerve stump by direct insertion into the nerve ends. Along these guide lines the growth of the nerve progressed in straight, parallel lines. The authors conclude that "aside from technical failures, excellent nerve regeneration was obtained by blood bridges. Functional recovery and histological appearance proved that in many cases the results were not inferior to those after end-to-end union."

TOZER, Philadelphia.

AFFERENT CONDUCTION VIA THE SYMPATHETIC GANGLIA INNERVATING THE EXTREMITIES. F. D. THREADGILL, Surgery **21**:569, 1947.

Threadgill proposes experimentally to justify his assumption that sensory impulses from the extremities are relayed in part to the sympathetic ganglia on their way to the spinal cord. Dogs were used as experimental animals. In the first experiment, after the preliminary removal of the sympathetic ganglia innervating one lower extremity, bilateral section of the posterior roots was performed of sufficient extent that no painful responses were elicited on the sympathectomized side. Identical stimulation of the animal's foot pads on the nonsympathectomized side with flame produced a response manifested by kicking, suggesting that at

least a portion of the painful sensation travels in the sympathetic ganglia. A second experiment was performed to rule out the possibility of sensation entering the spinal cord via the anterior root. Unilateral sympathectomy was followed by bilateral section of both the anterior and the posterior roots. The surgical procedure was sufficiently extensive to eliminate response on the sympathectomized side to the stimulation produced by the injection of lactic acid into the femoral artery on that side within a fifteen second period of observation. The artery had been ligated distal to the injection. Injection of lactic acid into the distally ligated femoral artery on the nonsympathectomized side immediately produced a sudden and pronounced fall in blood pressure. The author believes that vascular reflex response may be completed entirely outside the cord.

FRANKEL, Philadelphia.

METABOLIC FACTORS AFFECTING FIBRILLATION IN DENERVATED MUSCLE. B. FEINSTEIN, R. E. PATTLE and G. WEDDELL, J. Neurol., Neurosurg. & Psychiat. **8**:1 (Jan.-April) 1945.

Feinstein, Pattle and Weddell studied fibrillations by means of action potential records in denervated muscles of rats, guinea pigs, rabbits, an adult rhesus monkey and one of the authors. They found that motor unit action potentials could be elicited immediately after denervation, followed in two to sixteen days by fibrillation action potentials, at first mechanically induced and later spontaneous in origin. The spontaneous fibrillations gradually increased in number and continued until about two weeks before the reappearance of motor unit action potentials in the reinnervated muscles. Functional recovery did not occur until some time after the reestablishment of motor unit activity.

The time course of the fibrillations depends on the size of the mammal, the smaller the mammal, the earlier being the onset. Thyroidectomy tends to delay, and feeding with desiccated thyroid to decrease, the time before onset of fibrillations in rabbits. The number of fibrillations depends on the temperature of the denervated muscle, being increased by warmth and decreased by cold. In evaluation of the effect of drugs on fibrillations, the temperature of the muscle must remain constant. Atropine has no effect on the fibrillations; quinine and quinidine sulfate abolish them, whereas acetylcholine and neostigmine temporarily increase their activity. Muscular atrophy can be detected in man before the onset of fibrillations, indicating that they are independent phenomena. The study suggests that a metabolic factor is concerned in the activity of the fibrillations following denervation. The method of recording action potentials with concentric needle electrodes offers a valuable means of detecting the presence of minimal lesions of motor nerves and their subsequent regeneration.

N. MALAMUD, San Francisco.

RELATION BETWEEN FIBRE DIAMETER AND ACTION POTENTIAL OF SINGLE NERVE FIBRES. HELGE HERTZ, J. Physiol. **104**:1P, 1945.

Hertz studied the amplitude and form of the action potentials in single fibers of the frog's sciatic nerve when exposed to solutions of sodium chloride of varying composition and concentration. Exposure to hypertonic and hypotonic solutions of sodium chloride produced no change in diameter of the nerve fiber or in the action potential during the first ten minutes. Later the nerve shrank or swelled, and the declining phase of the action potential became progressively slower, until after exposure for one-half hour, although the nerve had returned to its previous diameter, the negativity persisted indefinitely after application of a stimulus. In isosotic solutions with six to ten times the normal potassium chloride content, there

was an immediate and reversible reduction in the amplitude of the action potential; its shape remained normal. Removal of calcium by citrate or oxalate caused spontaneous activity only after three quarters of an hour of exposure. Magnesium chloride and acetylcholine chloride were without effect.

The author concludes that the experiments demonstrate the relative impermeability of the membrane around the axis-cylinder. It appears unlikely that any great exchange of ions could take place in the short time required for the action potential to reach its maximum. The immediate effect of potassium chloride shows that it acts on the surface, but a normal $K^+ : Ca^{++}$ ratio within the membrane is necessary for the surface phenomenon.

THOMAS, Philadelphia.

NEUROGENIC FACTORS IN TRAUMATIC EXPERIMENTAL SHOCK AND EFFECT OF INTRACISTERNAL INJECTION OF POTASSIUM. S. OBRADOR ALCALDE and J. REMUS ARAICO, Bol. d. lab. de estud. med. y biol. **2**:121 (Sept.-Oct.) 1943.

Traumatic shock was induced experimentally in 7 dogs weighing 9 to 14 Kg. by repeated blows to the lower limbs with a leather-covered mallet (250 Gm.). There were about eighty blows a minute, and the duration of the trauma varied from one to six minutes. No fractures were produced. There was swelling at the site of injury in both lower limbs. Six of the dogs died from one to four hours and ten minutes after the injury; the average survival was two hours and ten minutes. In all these animals there were a gradual increase in the pulse rate and decrease in blood pressure and temperature with slight hemoconcentration. Autopsy showed pale viscera.

Six dogs, weighing 9 to 18 Kg. each, were traumatized in the same way except that in these animals a solution containing 4.87 mg. per cubic centimeter of a potassium salt was injected intracisternally during the trauma and at approximately hourly intervals afterward. Each animal was given two to four injections of 0.5 to 0.7 cc. of the solution. Four of the 6 animals recovered completely and were in good condition forty-eight hours after the experiments. Periods of excitement lasting up to twenty-five minutes were observed. The potassium caused an increase in blood pressure, bradycardia and tachypnea.

In 9 dogs the effect of intracisternal administration of potassium was studied after the animals were anesthetized with chloral hydrate. The blood pressure and respiration were watched carefully. The cardiovascular and respiratory responses already noted were not affected by decerebration at the level of the quadrigeminate tubercles. Section of the medulla at its junction with the cord resulted in absence of changes in blood pressure though the bradycardia persisted. When both vagus nerves were cut, the changes in blood pressure and respiration persisted, though no bradycardia was observed after intracisternal injection of the potassium solution. The authors believe that the intracisternal injection of potassium has a direct stimulating action on the vegetative centers in the medulla.

N. SAVITSKY, New York.

Neuropathology

EFFECTS OF VITAMIN AND HORMONE TREATMENT ON SENILE PATIENTS. P. E. VERNON and M. MCKINLAY, J. Neurol., Neurosurg. & Psychiat. **9**:87 (July) 1946.

Vernon and McKinlay tested psychologically small groups of senile patients who were treated with small and large doses of preparations of the vitamin B complex and vitamin C, and with androgens. The patients were tested individually

with a large battery of mental and psychomotor tests, both before and during each phase of treatment, and the results were compared with the results for a similar number of untreated controls. On the whole, the results showed that any changes brought about by vitamins or hormones were small and were often negligible. Certain psychologic functions, however, were favorably affected in some types of patients; others, in other types. The authors found that moderate doses of vitamins may improve general mental ability in cases of advanced senility and may produce some increase in fluency and decrease in perseveration in cases of light and moderate senility. Even these changes, however, amounted to only about 10 per cent improvement. At a later testing, after treatment with increased doses of vitamins, the effects were reduced, instead of becoming more prominent. Treatment with androgens produced no effect. Psychomotor tests and tests of intellectual deterioration failed to show any beneficial results. In the opinion of the writers, the lack of clearcut effects of treatment may have been due to the small series of patients tested, to the fact that the patients were already on a diet adequate in vitamins and to the unreliability of some psychologic tests.

N. MALAMUD, San Francisco.

PROGRESSIVE BULBAR PARALYSIS AND ITS RELATION TO CHRONIC POLIOMYELITIS AND AMYOTROPHIC LATERAL SCLEROSIS. HANS RUDOLPH STAEHELIN, Schweiz. Arch. f. Neurol. u. Psychiat. **52**:270, 1943.

A woman aged 63, who had been receiving treatment for myxedema during the preceding eleven years, died of bronchopneumonia fifteen months after the onset of progressive bulbar paralysis. Fibrillary twitching was observed in the muscles of the extremities a few months before death, but there was no associated atrophy. The tendon reflexes were hyperactive, particularly on the left side. Microscopic study of the thyroid gland, which was small and fibrotic, revealed lymphocytic infiltration and extensive regressive changes in the parenchyma. The entire brain stem was involved in an inflammatory process characterized by lymphocytic infiltration of the leptomeninges, perivascular cuffing, proliferation of glial cells and destruction of ganglion cells with neuronophagia. These changes were more pronounced in the tegmentum pontis than in the midbrain and were most intense in the medulla oblongata. Destruction of ganglion cells was observed in the reticular formation as well as in the nuclei of the cranial nerves, including the dorsal nucleus of the vagus and the vestibular nuclei. The lymphocytic infiltration within the brain stem was not entirely confined to the adventitial spaces, and small groups of extravasated red blood cells were observed. Sections from the spinal cord showed beginning degeneration of the lateral and anterior corticospinal tracts; these changes appeared first immediately below the pyramidal decussation. Early regressive changes in the anterior horn cells and the cells of Clarke's column were not accompanied with neuronophagia.

Staehelin expresses the belief that amyotrophic lateral sclerosis does not have a uniform cause. A number of cases have been reported in which perivascular infiltration was observed within the spinal cord and brain stem. The case he reports is unique in that bulbar paralysis was due to chronic polioencephalitis with pathoanatomic features strongly suggestive of Heine-Medin disease, whereas the accompanying symptoms of early amyotrophic lateral sclerosis were apparently due to purely degenerative changes within the spinal cord.

DANIELS, Denver.

GRANULAR ATROPHY OF THE CEREBRAL CORTEX: SYSTEMATIC FORM. FERDINAND MOREL and GILBERT MEYRAT, Schweiz. Arch. f. Neurol. u. Psychiat. **53**:316, 1944.

In a series of 600 brains, Morel and Meyrat found 8 cases of granular atrophy of the cerebral cortex. In the nonsystematized type of this condition, the lesions are scattered in an irregular fashion over the convex surfaces of both hemispheres and are often associated with larger areas of softening. In the systematic type, which is the subject of this presentation, the distribution of the lesions is symmetric in the two hemispheres. A bandlike area of granular atrophy extends back from the frontal pole along the middle frontal convolution to the central gyri, along which it ascends to the junction of their middle and superior thirds, whence it extends back along the superior parietal lobule. From the parieto-occipital fissure the band continues downward over the lateral aspect of the occipital lobe to the third temporal gyrus, which it follows forward to the temporal pole. The cortical areas involved are those in which the sylvian artery enters into anastomotic relations with the anterior and posterior cerebral arteries.

Although, as in 1 of the authors' cases, granular atrophy of the cerebral cortex may be due to thromboangiitis obliterans of the Winniwarter-Buerger type, arteriosclerosis does not appear to be an important factor. In cases in which organic disease of the cerebral arteries was lacking, vasospasm, capillary stasis, cardiac insufficiency and anoxia have been considered as causative agents. Microscopically, the condition is characterized by small foci of ischemic necrosis which generally involve two or three cortical layers. Retraction of the resulting glial scar gives rise to the characteristic pitting of the cortical surface. The clinical signs, such as agraphia, transitory aphasia, fleeting sensory and motor disturbances of monoplegic distribution, are seldom pronounced.

DANIELS, Denver.

Psychiatry and Psychopathology

THE PSYCHOLOGICAL APPRAISAL OF CHILDREN WITH NEUROLOGICAL DEFECTS. E. MEYER and M. SIMMEL, J. Abnorm. & Social Psychol. **42**:193 (April) 1947.

Meyer and Simmel believe that the psychologic examination of children with neurologic disorders must be qualitative and descriptive in order to become meaningful for differential diagnosis, as well as for prognosis and therapy. The prevailing quantitative test methods should be supplemented by an orientation and/or by procedures based on genetic studies of reasoning and attention. Three groups of patients are discussed. 1. Children with impairment since birth who are predominantly characterized by a lag in development of the processes of abstraction. The typical psychometric picture is that of superiority of performance items over verbal items. In the field of performance, they are at their best with simple form board items. 2. Children who have apparently developed normally up to the time when they suffered a severe injury or disease. These children show a discrepancy between their present inadequate level of functioning and the level of achievement attained prior to the impairment. Children with a severe head injury or rapidly developing neoplasm have a stock of information acquired prior to the acute insult which is almost completely intact and is easily activated under certain conditions. They have serious difficulties in reasoning and learning. In the group recovering from encephalitis the basic defects are essentially the same, but their ability to learn is impaired even more seriously by lack of concentration of attention.

3. Children with recurring seizure-like states, who periodically experience loss of effective contact with the environment. The distinctive feature is the periodic fluctuation in the quality of the child's performance during a given examination or between examinations given at varying intervals. FRANKEL, Philadelphia.

LOSSES AND GAINS IN COGNITIVE FUNCTIONS AS RELATED TO ELECTROCONVULSIVE SHOCKS. C. P. STONE, J. Abnorm. & Social Psychol. **42**:206 (April) 1947.

Stone studied the effects of electroconvulsive shock on cognitive functions in psychotic patients, as assessed by the Wechsler memory scales. The subjects were mainly schizophrenic patients with an illness of relatively short duration. Group 1, composed of 15 patients, took form I one day before their first shock and form II one day after their last shock. The total number of shocks received differed. The loss in memory quotient was 15.1 per cent of the initial score. Group 2, consisting of 14 patients, took form I one day after their last shock and form II slightly more than two weeks thereafter. This group afforded a basis for estimating gains during the "period of rapid recovery from amnesia." The mean gain in memory quotient was 27.9 per cent of the score on form I. The author has established that the trend of test scores on cognitive function is downward as psychotic patients receive a series of convulsive shocks and is upward in the post-shock period. However, the losses and gains cannot be related to the patients' normal levels of intellectual ability, nor can there be determined the proportion of losses or gains which should be ascribed to cortical injury resulting from the electroshock, as opposed to the factor of mental illness or exacerbations of symptoms associated with treatments. FRANKEL, Philadelphia.

THE USE OF RELAXATION IN SHORT-TERM PSYCHOTHERAPY. G. R. PASCAL, J. Abnorm. & Social Psychol. **42**:226 (April) 1947.

Pascal describes a technic of short term psychotherapy in a series of 12 patients in which treatment hours ranged from three to thirteen. The approach was one of enlisting the active participation of the patient; active, direct probing by the patient and the therapeutist; judgment as to the source of difficulties; facilitation of recall by relaxation; promotion of insight, and readjustment. Ten patients showed improvement with this treatment; the results for the other 2 were inconclusive. The author feels that this approach assists the patient in terms of his specific areas of maladjustment and effects recovery from neurotic symptoms so that the patient can carry on with the tasks of his normal living. It does not free the patient entirely of his anxieties, nor does it effect profound personality changes. The author does not recommend it as a substitute for psychoanalysis or any other long term psychotherapy. FRANKEL, Philadelphia.

NATURE AND CLASSIFICATION OF THE SO-CALLED PSYCHOSOMATIC PHENOMENA. OTTO FENICHEL, Psychoanalyt. Quart. **14**:287, 1945.

Fenichel does not approve of the expression "psychosomatic" because every disease is psychosomatic, since no "somatic" disease is entirely free from "psychic" influences. However, between the nature of diseases which arise from purely physical and chemical causes and the field of conversion there lies a large field of problematic functional, and even anatomic, alterations, and it is this field which Fenichel wishes to clarify. He first defines what is meant by conversion, i. e., functional changes occurring in the body which are distorted expressions of wishful

thoughts or fantasies. Not all somatic changes of a psychogenic nature are of this kind. Unconscious instinctual attitudes may influence organic functions in a physiologic way without the changes having any definite psychic meaning. This is now called psychosomatic, but was formerly called organ neurotic.

Fenichel distinguishes four classes of organ neurotic symptoms: 1. Symptoms which are affect equivalents. In these the physical expressions of an affect are experienced, even though the person succeeds in warding off the recognition of their affective significance. This blocking of awareness is the simplest form of defense against affects. Affect equivalents may arise also when an emotion has become associated in childhood with a certain physical attitude, the latter being used in later life as a distorted expression of the emotion in question. As affect equivalents have a diminished discharge value, the affective attitude may become chronic, and symptoms created by the chronic affective attitudes may cease to be purely affect equivalents and come to belong to the next category.

2. Symptoms resulting from changes in the chemistry of the unsatisfied and dammed-up person. Theoretically all psychoneuroses could be described as a subcategory of symptoms due to the disturbed chemistry of the dammed-up person. This organic basis of the average psychoneurosis is entirely hypothetic, whereas certain physical symptoms of "unconscious" or "strangulated" affects are now accessible to research. "Unconscious affects" apparently cause quantitatively and qualitatively different hormonal secretions and in this way influence the vegetative nervous system and the physical functions.

3. Symptoms which are the physical results of unconscious attitudes. An unusual attitude which is rooted in unconscious instinctual conflicts causes a certain behavior. This behavior, in turn, causes somatic changes in the tissues. The changes are not directly psychogenic, but the person's behavior which initiated the changes was psychogenic; the attitude was intended to relieve the internal pressure; the somatic symptom which was the consequence of the attitude was not sought by the person, either consciously or unconsciously.

4. All kinds of combinations of these three possibilities. In conclusion, Fenichel comments on the applicability of psychoanalysis as a therapy in the states discussed. The great variety of the phenomena here examined makes any general statement impossible. There are states which have become "organic" to such an extent that immediate physical treatment is necessary. But whenever symptoms are the outcome of chronic or unconscious attitudes, psychoanalysis is indicated for the purpose of making this attitude conscious and thus overcoming it. Symptoms of organ neurosis are not "directly accessible" to psychoanalysis. Indirectly they are. If the anxiety or other obstacles which hinder the adequate discharge of a person's impulses are removed by analysis, the indirect symptoms disappear without having been made a specific object of psychoanalysis. The change in the function cannot be "analyzed" because it has no unconscious meaning; however, the attitude which produced it *can* be analyzed, and if the attitude is given up, or the state of being dammed up is overcome, involuntary consequences likewise disappear.

How much can be achieved through shorter, nonanalytic methods of psychotherapy is a question not to be answered without a detailed discussion as to what the really effective mechanisms of these nonanalytic psychotherapies are, a question which can be answered only by means of psychoanalytic theory.

PEARSON, Philadelphia.

RECENT TRENDS IN ALCOHOLISM AND ALCOHOL CONSUMPTION. E. M. JELLINEK, Quart. J. Stud. Alcohol **8**:1 (June) 1947.

Jellinek has prepared an elaborate statistical analysis intended to answer questions which are on the public mind concerning alcoholism and the consumption of alcohol. He has determined that the per capita consumption of alcoholic beverages, based on the population of drinking age, rose steadily in the course of World War II but remained below the level of the preprohibition years. The 1940 to 1945 trend was not a continuation of the trend of the preceding five years but was a new trend, determined by war factors. The rise in consumption during this period was due to an increase of 35 per cent in the number of consumers, but individual consumption hardly increased. Since 1850, the per capita consumption of distilled spirits has decreased by 53 per cent, whereas the per capita consumption of beer has increased by 862 per cent.

The estimated number of persons with chronic alcoholism per hundred thousand of the adult population was greatest at the beginning of this century, was less between 1915 and 1930 and then again began to increase, but the level remained well below that of 1910. The rate of chronic alcoholism for women was greater in 1910 than in 1945; the rise in the rate for women during the postprohibition years was much less than the rise in the rate for men. The rate of chronic alcoholism in cities of 100,000 and more inhabitants is higher by 33.7 per cent than that in the smaller cities and higher by 105 per cent than that in rural areas. The entire increase in the rate of chronic alcoholism since 1930 has appeared in urban areas. In 1944, California had the highest rate of persons with chronic alcoholism; South Carolina had the lowest. San Francisco had the highest rate of all large American cities. There is no indication of a shift in age for full-fledged alcoholism, either in terms of age at death from alcoholism or in terms of age at time of first admission for alcoholic psychoses to a hospital for mental disease.

FRANKEL, Philadelphia.

THE PROBLEM OF GAINING COOPERATION FROM THE ALCOHOLIC PATIENT. H. M. TIEBOUT, Quart. J. Stud. Alcohol **8**:47 (June) 1947.

Tiebout analyzes his approach in eliciting the cooperation of the alcoholic patient so that treatment may begin. Initially the patient is aroused to the existence of a problem in his drinking; the therapeutist's function is to create an uneasiness in the patient about his alcoholic way of life. The second stage in securing cooperation involves helping the alcoholic patient to learn that his own methods of solving his problem will not succeed. Characteristic of this stage is the growing uneasiness developing in the patient, the discomfort becoming sufficiently severe as to make him unable to bear the tension. He also acquires the conviction that he cannot solve his problem unaided. In the third stage, under the impetus of a full realization of his inevitable deterioration as a human being and his utter powerlessness to stop that process, the patient turns to another source of assistance in combating his condition. In the third stage, the patient has become cooperative and amenable to treatment.

FRANKEL, Philadelphia.

THE USE OF CONTENT ANALYSIS IN RORSCHACH INTERPRETATION: I. DIFFERENTIAL CHARACTERISTICS OF MALE HOMOSEXUALS. FLOYD O. DUE and M. ERICK WRIGHT, Rorschach Research Exchange **9**:169 (Dec.) 1945.

Due and Wright stress the importance of the content analysis of responses to the Rorschach test as an aid in differential diagnosis and in revealing significant psychodynamic factors in the genesis of homosexuality. They find the following types of response to be characteristic of male homosexual subjects:

1. Derealization, accomplished by (*a*) mythical distortion, (*b*) qualifications toward the abnormal or (*c*) dehumanization

2. Confusion of sexual identification, by (*a*) double identification, (*b*) uncertainty or (*c*) evasiveness

3. Feminine identification, by (*a*) specification of feminine gender, (*b*) projection of "feminized" behavior or (*c*) preoccupation with feminine apparel

4. Castration and phallic symbolism

5. Sexual and anatomic responses

6. Esoteric language and artistic references

7. Paranoid reactions

Although in no single case may all these content factors appear, the presence of many should be considered significant in diagnosis.

MARCOVITZ, Philadelphia.

SPASMODIC TORTICOLLIS: RESULTS OF PSYCHOTHERAPY IN TWENTY-ONE CASES. M. T. PATERSON, Lancet **2**:556 (Nov. 3) 1945.

Paterson attempts to assess the etiologic factors in spasmodic torticollis. She asserts that it has never been easy to determine how far this condition is of psychogenic origin or how far it is more closely allied to the structural disorders, with a lesion in the extrapyramidal system. In many instances the one condition dovetails into the other. In the literature, statements are found to the effect that in some cases spasmodic torticollis may be associated with lesions in the corpus striatum. Paterson states that in treatment of the simple hysterical form psychotherapy has been widely used, with fair results, but that the spasm of true torticollis responds little, if at all. Mechanical immobilization with a plaster cast or brace may produce immediate relief, but the effect is never permanent. Some authors have stressed the importance of removing foci of infection. Sedatives have little effect. Neurosurgical measures have been employed with increasing frequency in the relief of spasm.

The author presents a survey of 21 cases; in 18 the disorder was considered psychogenic, and in 3, of possible organic origin. Psychotherapy, which was used with all patients, led to cure in 5 cases, to great improvement in 5 cases and to slight improvement in 7 cases; in 4 cases the patient's condition was unchanged on his discharge from the hospital. A detailed analysis was made of the setting in which the torticollis first developed. The patient's dominant drives and interests and emotional reactions and attitudes at that time were investigated. In intelligent and cooperative patients good resuls were achieved by giving them insight into, or an explanation of, the way in which the torticollis had arisen. With patients of poor intelligence recourse was had to suggestion, which also plays a part in insight or explanation. The influence of suggestion was much enhanced by induction of a mild hypnotic or narcohypnotic state.

Paterson concludes that, except in cases with gross signs of organic disease, psychotherapy is the method of choice.

YASKIN, Camden, N. J.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Kenneth J. Tillotson, M.D., *Presiding*

Regular Meeting, May 16, 1946

Address of Welcome. COLONEL F. V. KILGORE, Medical Corps, Army of the United States.

A year ago, when it was my pleasure, on the part of my colleagues and myself, to welcome you to Cushing General Hospital, the neurologic and neurosurgical sections were chiefly concerned with the problem of peripheral nerve injuries, since our wards were then filled to overflowing with patients with such injuries In fact, it has been estimated that 15 per cent of all casualties evacuated to the Zone of the Interior had an injury to one or more peripheral nerves. During the past year important studies have been completed on the management of these lesions and many data obtained concerning the rate of growth of peripheral nerves after suture in various locations. A technic of intraneural electrical stimulation has been devised which allows an accurate assessment of the probable future course of nerve regeneration considerably sooner than would be the case if it were necessary to await the return of voluntary muscle function. Of this more will be heard later.

Peripheral nerve surgery occupied most of our time last year. The follow-up observation on the old nerve injuries and sutures remains a considerable undertaking because of the time required for recovery and the replacement of patients discharged from this hospital by postoperative patients transferred from other Army hospitals which are closing. Patients with peripheral nerve injuries still constitute over 50 per cent of the total, but their care is now chiefly nonsurgical.

The places of a number who have returned to duty or to civilian life have been filled with their less fortunate brothers who have sustained penetrating or other wounds of the skull and have subsequently become the victims of convulsive seizures, in addition to their paralyses, hemianopsias, aphasias and other disorders. An intensive program of study has been underway on this group of patients since Dec. 1, 1945. Careful clinical examination, together with electroencephalography and the use of small doses of anticonvulsant drugs, has led to the partial localization of the epileptogenic focus in many of those patients whose seizures have not been adequately controlled by medication. Direct application of electrodes to the surface of the brain with the stimulation of exposed brain by a weak electric current at the time of craniotomy has often revealed the precise gyrus or gyri which were giving rise to the convulsive seizures and has enabled the neurosurgeon to ablate these areas with considerable accuracy. Thus far the immediate results appear satisfactory. Only time, of course, will determine conclusive results. Of this and other matters you will hear from the men who have been engaged in the work.

Again, may I welcome you to Cushing General Hospital.

Intraneural Stimulation. CAPTAIN FRANK E. NULSEN, Medical Corps, Army of the United States.

Problems in Post-Traumatic Epilepsy. MAJOR A. E. WALKER, CAPT. F. A. QUADFASEL, CAPT. C. MARSHALL, CAPT. M. G. NETSKY, CAPT. R. G. FISHER and LIEUT. I. C. KAUFMAN, Medical Corps, Army of the United States, and LIEUT. J. W. GERHARDT, Women's Army Corps, Army of the United States, with the technical assistance of E. N. BERESFORD.

Approximately 25 per cent of soldiers receiving penetrating wounds of the brain in World War II have had convulsive seizures within the first year or two after their injury. In order to study their cases in detail and formulate a rational method of treatment, such patients have been collected at Cushing General Hospital.

Detailed medical and social histories were obtained. Neurologic and electroencephalographic examinations were carried out in all instances. In approximately 75 per cent of the cases the convulsive manifestations were controlled by medication. The drugs used included phenobarbital, diphenylhydantoin and trimethadione N. N. R. ("tridione").

In cases in which the attacks persisted in spite of the medication, an effort was made to determine the exciting focus so that surgical therapy might be instituted. Although in approximately 80 per cent of the cases abnormalities appeared in the electroencephalogram, the majority of these abnormalities were of the nature of foci of slow waves in or about the area of the wound and could not be correlated with the exact epileptogenous focus.

In order to determine more accurately the epileptogenous focus, a number of convulsant agents, or agents which modified the electroencephalogram, were employed. These agents are tabulated as follows:

Activation of Electroencephalogram

Agent	No. of Cases	Effect
Penicillin (10^5 units intravenously)	5	None
Sodium amytal or pentothal (0.25-0.5 Gm. intravenously)	5	Fast, sharp waves
Sodium cyanide (0.3-0.4 mg./Kg. intravenously)	17	Slow waves
Acetylcholine (100-300 mg. intravenously)	18	None
Alcohol (40-150 cc. of 10 per cent alcohol intravenously)	16	Sedation
Hydration		
1,000 cc. isotonic solution of sodium chloride	1	None
5,000-6,000 cc. and pitressin	8	None except marked nausea and vomiting
Hyperventilation	..	Inconclusive
Electric stimulation (200 ma. for 0.05-0.15 sec. or 2-5 ma. for 2-3 sec.)	11	None
Trimethadione (50-100 mg. in 5 per cent isotonic solution of sodium chloride)	18	None
Metrazol (2 cc. intravenously)	93	62 electroencephalographic alterations

Metrazol Activation of Electroencephalogram

	No. of Cases
Intravenous administration (2 cc.)	93
Generalized seizures	12
Electroencephalographic changes	
Generalized	12
Localized	50
Intramuscular administration (6 mg./Kg.)	11*
Generalized seizures	1
Electroencephalographic changes	
Localized (one became generalized)	2

* Of these 11 cases, 2 cc. of metrazol was given intravenously in 9, and localized electroencephalographic changes appeared in all.

Of these various agents, metrazol was found to be the most effective in producing activation of the epileptogenous focus. Approximately 60 per cent of

patients whose electroencephalogram was activated by metrazol showed electroencephalographic abnormalities indicative of convulsive manifestations. These abnormalities were sufficiently localized, at least initially, that the position of the focus relative to the site of cerebral injury could be determined. On patients whose convulsions were not controlled by medication after the focus had been definitely determined by metrazol activation, cortical exploration was carried out.

Electrocorticograms usually showed relatively little abnormality other than slow waves from the vicinity of the cerebral scar. Activation of the cortex by subclinical and subconvulsive electrical stimulation brought out an area of cortex which showed epileptogenous activity for many minutes, in some cases as long as twenty-eight minutes after the activation. Such epileptogenous zones were adjacent to, but not within, the cerebral scar. In a few instances multiple epileptogenous foci were found about the scar.

Various surgical technics were employed in dealing with the epileptogenous focus and cerebral scar. In approximately one fifth of the cases the scar was resected. In another fifth the scar was resected to the cerebral ventricle and fragments of bone in the brain were removed. In approximately one half of the cases only the epileptogenous focus was removed by subpial dissection, without any attempt being made to remove the cerebral scar. After removal of the epileptogenous focus, the completeness of the ablation was checked by activated electrocorticograms.

It is much too early to know the results of the operative procedures which were carried out, but to date the results have been encouraging.

DISCUSSION

D. DENNY-BROWN: I am sure that all of us appreciate not only the great interest of Major Walker's presentation, but the originality of his methods of approach. Major Walker and his colleagues have devised a comprehensive program, which promises not only to do a great deal for patients with peripheral nerve injuries but to give accurate information and analysis of the process that underlies post-traumatic epilepsy. The procedure of seeking an induced electrical change as an index of abnormality particularly appeals to me. The localization of an aura of a jacksonian attack, though extremely useful and apparently accurate in localizing the focus of an attack, was helpful only in cases of frontoparietal lesions which involved the sensorimotor cortex. With electrical stimulation, Dr. Penfield and his associates had extended this to excite convulsive discharge to some neighboring gyri Major Walker's method widens one's ability to define the focus consistently; and, as I understand him, in approximately 100 per cent of cases with scars he can now define a focus of electrical activity which gives every promise of being a focus of epileptic activity. The method of excision should in time provide valuable information as to the significance of these disorders in excitability in relation to the epileptic state.

I should like to ask Major Walker particularly what evidence he has gained so far that the focus is a stable one. In electroehcephalographic studies epileptic foci had seemed to move within the general region of the scarring, particularly when the scar was a large one.

As Major Walker has already stated, the fit obviously begins in abnormal neurons, and not in the fibrous tissue of the scar. The application of the theory of Forster and Penfield that traction of the scar tissue was the important factor led to difficulties in defining traction and the area it affected. Structural abnormalities in surviving nerve cells, altered blood supply and states of partial anoxia are difficult to assess, particularly in the living subject. The study of electrical

excitability offers an objective and direct approach in terms of altered physiology which may change the whole concept of scars and the way in which they produce epilepsy.

DR. WILLIAM H. SWEET: I shall not comment at length on this brilliant piece of work, but I should like to mention a pertinent point in my personal experience. Protracted postoperative anticonvulsant medication is an important part of treatment in cases of post-traumatic epilepsy. Dr. Walker has already emphasized this type of preoperative medication. I have in mind a patient on whom I carried out an extirpation of the frontal pole, including a huge frontal scar. The patient had no seizures for one year, during which medication was eliminated. Several months after all anticonvulsants had been stopped, she went into status epilepticus and nearly died. I now give this and similar patients anticonvulsant medication at least two years after operation, even if they have had no more seizures.

I have had the privilege of watching Dr. Walker perform one of his operations reported on this evening. I wish to compliment him on the meticulous care with which he made these exposures, which involve much tedious dissection. A particular pitfall is the surgeon's tendency to tire before exposing a broad area of brain all around a large scar. This carries with it the danger of overlooking one or more foci lying beyond the surgeon's exposure. Unless an extensive blanket of electrodes is used over areas all around the scar in cases with no clinical or electroencephalographic clue to a consistent focus of origin of the seizures, multiple electrical foci may well be missed.

DR. JOHN A. ABBOTT: At the Cushing General Hospital one sees a great many cases of a type seen only rarely in the brain wave laboratory at the Massachusetts General Hospital. In these cases there have been cortical lacerations, and the electroencephalograms show spiking activity at or near the wound. Such cases are commonplace in the brain wave laboratory at the Cushing General Hospital and Dr. Kibbe had any number for display when I visited the laboratory last year.

Despite the active brain surgery at the Massachusetts General Hospital, such cases are so rare as to constitute museum pieces in the brain wave laboratory there. In fact, of the 6,000 or more patients whom my colleagues and I examined in the past four years, I can recall only 1 in whom such a focus was demonstrated. In his case the focus was typical, the cortical scar was excised and, again typically, the focus had disappeared on reexamination and the patient had continued to be free from seizures for a year or two since excision of the cicatrix.

It is interesting to see that surgical and laboratory experience can be so different in different institutions, but this difference of experience makes it difficult to contribute much of worth in discussing the electroencephalographic aspect of Dr. Walker's brilliant paper. In the sample electroencephalograms, of which Dr. Walker has been able to show us an abundance, one sees at the epileptogenic focus such high voltage, fast activity as Dr. Lennox and the Gibbses have said is characteristic of grand mal. Again, their intensive experience with epileptic patients studied during seizures have enabled them to make an observation which others are so rarely able to confirm that the observation is sometimes treated with skepticism and the electrocortical activity which they report is sometimes rejected by others as nothing more than a record of muscle potentials. The electrocorticograms of which we have seen so many examples in this presentation would seem to support the correctness of their observation that such activity is characteristic of grand mal seizures and so would seem to establish the brilliance of their generalization.

DR. ROBERT S. SCHWAB: This study is an extraordinary contribution to the surgical treatment of epilepsy. It is with great admiration that I have seen this

demonstration and the operating room technic. My colleagues and I had the privilege of borrowing for one day the electrode holder for an operation of Dr. Mixter's, and we were all impressed with its efficiency. The importance of this work is that it is another step in the breaking down of idiopathic epilepsy. Seizures involving one side of the body, described by Hughlings Jackson in 1870, were the first portion of this unknown pathologic process to be explained and understood. The electroencephalographic work of Gibbs and others led to the location of foci which were not seen clinically, and another portion of unexplained, or idiopathic, epilepsy was uncovered for surgical therapeusis. Patients were operated on and tumors or scars were removed which were not seen clinically. Now, a more refined method is available for further localizing the lesion and for removing it. Major Walker has driven a further wedge into the differentiation of states which are called generalized epilepsy and has further narrowed the zone of darkness about the etiology of epileptic seizures. This is a new era, with a new method of handling epilepsy, and I am sure it will benefit many sufferers from this malady that could not have had much hope for relief of their seizures with ordinary surgical procedures.

Dr. Leo Alexander, Durham, N. C.: Dr. Woodhall and I (*Tr. A. Neurol. A.* **68**:175, 1942) described biopsies of epileptogenic lesions of the calcified variety. We described the formation of abnormal vascular sinusoids, or giant capillaries, in some cases and of an abnormally tenuous capillary net in others. All these cases had one thing in common—an awkward blood supply. We correlated this with the observations of Gibbs and Lennox, who stated that a high carbon dioxide content of the blood was a contributing factor in the mechanism of seizure production. I should like to ask whether biopsy specimens were studied with the benzidine stain and whether abnormal capillaries were seen.

Dr. Augustus S. Rose: I should like to know whether the location of the scars is a factor in determining whether the anticonvulsant drug will be effective.

Major A. E. Walker, M. C., A. U. S.: I appreciate the discussion which has followed this paper. In many cases the discharging focus remained in one place for one to three and one-half hours. The focus was stimulated intermittently over a period of an hour and consistently gave rise to epileptic discharges, whereas adjacent areas did not give rise to such responses. Yet in 1 case we followed a focus as it moved from a point below to a point above the scar in a period of twenty-eight minutes. In the majority of cases the focus is fixed. When migration occurs, it is about the scarring, not radially.

The role of scar traction in the production of epileptic attacks has received much attention. If that is the responsible factor, there is no reason that every patient who has a scar should not have convulsive attacks; but at least half of them do not.

Dr. Denny-Brown asked why the nerve cells above the scar give rise to epileptic seizures. I do not know. I think it has to do with the functional organization of the cortex after injury. In monkeys in which a coil has been placed beneath the scalp and repeated epileptic attacks have been induced, it is difficult to produce the discrete movements characteristic of area 4 by stimulation of the cerebral cortex because clonic discharges result from minimal stimulation. I think that the problem is concerned with the functional reorganization of the cortex rather than with the pathologic process per se.

After operation the patients continue to receive anticonvulsant medication, but in smaller doses than before operation. Many take only 3 grains (0.195 Gm.) of phenobarbital daily.

It is often impossible to expose all of a large scar because of serious bleeding We have been relying on our electroencephalogram to locate the focus superior inferior or lateral to the cranial defect. On that information we plan the bone flap. In some cases we may overlook a focus, especially if there should be more than one. To date, we have always found the focus where the electroencephalogram located it. We have found more than one focus in some cases.

The activated electrocorticogram may be unassociated with any clinical phenomena, or it may be associated with the aura of the patient's attack. In some cases the aura has progressed to a clinical attack.

There is no difference to the naked eye between the scars in patients who have convulsive attacks and scars in patients who do not. The scar is composed of vascular, glial and fibrous tissue. The adjacent cortex contains abnormal, dark-staining neurons and glial tissue.

We have not been able to find the vascular abnormalities which Alexander and Woodhall described.

Kenneth J. Tillotson, M.D., *Presiding*

Regular Meeting, Oct. 17, 1946

Neurologic Effects of Blast Injury. DR. HANNIBAL HAMLIN.

Blast injury may be regarded as the total injury of total war. The explosive potentialities of ordnance equipment witnessed enormous increase during World War II. One can scarcely estimate the amount of energy in terms of heat, pressure or velocity produced by the explosion of an atomic bomb.

Blast injury does not constitute a medical entity. Rather, one should think of injuries to various organ systems associated with blast. Most of these injuries are caused by secondary effects of the explosion, and their pathologic character does not differ from that of civilian trauma. This study is concerned with primary effects on the nervous system, if any, of the three types of blast encountered, namely, atmospheric, immersion and solid blast.

The physical properties of blast deal with dispersal of energy in terms of time, distance, pressure and temperature. In atmospheric blast the forces of the positive pressure wave and its windage decrease roughly in proportion to the square of the distance from the center of the explosion. If an obstruction is met, reflectance causes a doubling of the pressure. These are the forces that bring about displacement of objects in their path, including the human victim, and it is the rapid movement or acceleration of the victim and the fate of his trajectory that produce most of the injuries, which are secondary, and not primary, to the explosion.

The pathologic effects of airborne blast have been duplicated in animals by Zuckerman, Williams and others, who found the central nervous system to be free of any consistent and typical damage. The pressure of an underwater explosion simulates a sound wave, its force being increased fourfold over that of a comparable atmospheric blast. In solid blast energy is transmitted through a metallic medium, which causes great intensification of the pressure peak. Corey, who worked on experimental blast for the Navy, proposed the term "explosion pressure"; so one may speak of explosion pressure in air or water or of ground shock or impact transmission through solids, whenever the meaning may be better conveyed.

Many victims of underwater blast with evident visceral injury also show signs of neurologic involvement. Hemorrhage within the leptomeninges and their sequelae

may occur Cerebral petechiae have been observed at necropsy. Although neurohistologic proof is far from complete, intracranial hemorrhagic changes have been described in experimental animals after bodily exposure to lethal immersion blast. Experiments rigged by Corey to eliminate secondary injury from fragmentation and reflectance in atmospheric explosion produced gross and microscopic lesions of the brain in 2 out of 7 specimens examined for neuropathologic changes.

Experimental intravisceral compression was studied in slow motion on dogs by Young. In his investigation, a measurable increase of pressure against the body wall was correlated with resultant augmentation of venous and intracranial pressure to extraordinary levels and with concurrent fall in arterial pressure. Solid organs in the visceral cavity may be contused and hollow organs ruptured, especially when containing gas, by rapid compression of the body wall. The rigid enclosure of the brain and spinal cord protects against direct extension of pressure, but indirect transmission to the neuraxis is possible through venous and meningeal channels. Such a mechanism may generate the primary effect of explosion pressure on the living subject, at least in immersion blast, in which the factors of secondary displacement and acceleration do not operate as under atmospheric conditions. Another possible cause of neurologic injury from submarine blast is damage to the autonomic ganglia within the visceral cavity, affecting cardiorespiratory and intestinal reflex arcs. Instances of delayed perforation of the intestine following blast contusion may be attributed to parasympathetic paralysis, which promotes stasis and compromises reparative processes. Histologic changes have been noted in ganglia removed from victims after death.

The pathogenesis of solid blast, as described by Barr, depends on the passage of force through the metallic structure of a ship from an adjacent submarine explosion and further transmission through a human subject in immediate contact. The shock wave traverses objects so rapidly that there is a lag between its delivery and the secondary displacement of material or persons in its path. In addition to fractures of the lower extremities and the spine, caused by secondary displacement, focal hemorrhages in the brain, due to the primary shock wave, have been observed in victims of solid blast.

Two other causes of death from blast injury with neurologic implications should be mentioned: air embolism by bronchovenous fistula and carbon monoxide poisoning following exposure to explosion within a confined space.

It is estimated that the majority of casualties produced by the atomic bomb explosions at Hiroshima and Nagasaki were caused by burns and secondary effects of blast; less than 10 per cent were attributed to other mechanisms. It would seem that the primary effect of blast on the human subject has been overemphasized, but the claims may have some basis in fact under certain conditions.

DISCUSSION

DR. D. DENNY-BROWN: There seem to be at least two fundamental questions involved in this subject of blast injury. The first is whether or not blast causes a specific kind of damage to the nervous system, different from known neuropathologic changes. The second is whether the mechanism of effects of blast is such that they may be avoided by special design of equipment. It seemed to me that all the neuropathologic effects presented by Dr. Hamlin are consistent with those of ordinary types of cerebral injury, due to direct transmission of physical changes to the brain, namely, contusion, petechial hemorrhage and perhaps concussion. Should such changes be set aside from other kinds of head injury? It is, of course, of interest to separate blast injuries in the sense Dr. Hamlin has described them from other kinds of head injury—of interest to designers of ships, helmets

and protective equipment, because designers wish to know the percentage and types of injuries to the central nervous system produced in circumstances of a particular kind so that they may take steps to minimize such effects. This aspect of the problem differs from that relating to prognosis and treatment. I am glad that Dr. Hamlin distinguished the secondary effects of blast injury from impact of the head against a solid object. Solid blast, as Dr. Hamlin described it, seems to me not to differ from concussion and severer types of head injury produced by falling from a height and landing on solid ground on the feet or buttocks, which causes injury to the base of the skull and the base of the brain. Concussion so produced differs in no way from striking the head against a solid object, or from striking the still head with a moving object. There is still a difference of opinion regarding the mechanism of production of petechial hemorrhages in the brain by immersion explosions.

I find it difficult to argue from the experiments made by Dr. Young, because the pressure on the thorax was produced slowly and a delay in rise in venous pressure occurred. This condition does not appear comparable to the sudden change in pressure produced by explosion. In the presence of so much pathologic change in the lung, thrombosis and the possibility of emboli reaching the brain have not been excluded as a cause of petechial hemorrhages.

Dr. Robert S. Schwab: My associates and I had some experience with blast in the Navy, but we had no electroencephalograms. I should like to mention a series of patients we had in the Pacific who were exposed to severe air blast. A group of "Sea Bees" were at a movie, sitting on a 1,000 pound (450 Kg.) Japanese bomb. One man played with a fuse while watching the movie, and the bomb exploded. About 8 men were sitting near the bomb, in a row. Four were blown to pieces; the other 4 were brought into the hospital. They had lacerations from fragments; 2 had no evidence of any other physical injury. The 4 men, after recovering from their wounds, were kept under observation for blast injuries. In none of the men were neurologic signs found. All the patients were sensitive to noises and startle phenomena, and all went back to the "Sea Bee" battalions.

When I was in the Naval hospital in Chelsea, in 1941, we had a number of survivors from the *Reuben James,* sunk before the country was in the war. One man was in the water when a series of depth charges were dropped by other destroyers, and he suffered from underwater blast. This man was sent in with a diagnosis of blast concussion under water. His case was interesting. He had a definite history of tarry stools after being brought out of the water, and there was slight hemoptysis. The neurologic status was normal. The main trouble was psychiatric. He could not sleep and was tremulous. In a series of interviews, he described a harrowing experience. He was in the water for hours in the cold Atlantic, near Iceland, so cold that he lost the feeling in his legs. He grasped an object in the dark and found it was a leg. He thought it was his own, that he had been cut off at the waist. For fifteen minutes he had terrible anxiety that he was transected in the middle and that the leg was his own. This story all came out after a series of interviews, without the use of narcosis or hypnosis. After this, he lost most of his psychiatric symptoms. We were then able to send him back to his base. This was a case which seemed, because of involvement of the intestine and lungs, to be one of underwater blast. A more careful and extended study of many patients who are brought into hospitals under pressure of war, with a history of many admissions, would reveal that a large percentage of symptoms are purely psychiatric. One of the mistakes made early in the war was that in the presence of physical injury one could exclude a psychiatric diagnosis. That is false. A good many neuroses are found in severely wounded sailors. A number of cases of

blast would fit into the psychiatric nomenclature. I agree with Dr. Denny-Brown that there is no need of having blast injury as a separate category. I think Dr. Hamlin and I agree on that. Blast, when one can exclude injury from displacement against solid objects, produces a psychiatric syndrome.

DR. JAMES C. WHITE: I have not seen any patients in the Navy or the Marine Corps with evidence of organic cerebral damage which could be definitely attributed to blast alone. I was in Oxford with Dr. Zuckerman in 1941, when he was studying the effects of blast on experimental animals. He used rabbits, animals with pliable thoracic walls. These animals were exposed to the blast of a 60 pound (27 Kg.) charge of high explosive at varying distances down to 9 feet (270 meters). These animals did not lose their corneal reflexes or show any evidence of concussion, but died within a few hours of pulmonary hemorrhage and edema. When the animal's thorax and abdomen were protected but the head was exposed, there was no evidence of injury with blast pressures of great intensity.

The man Dr. Hamlin mentioned who was blown across the deck might well have suffered sudden acceleration of his head in space from a direct blow or sudden arrest of his head in movement. Dr. Schwab and I saw the patient from the U. S. S. *Yorktown* with the intense anxiety and tremor whom Dr. Hamlin mentioned, as he was finally hospitalized at the Naval hospital in Chelsea. With his proximity to the blasts of three explosions and his repeated losses of consciousness, there is every reason to assume that he sustained an organic injury to his brain.

DR. PAUL B. JOSSMANN: Is there any resemblance to injuries caused by consistently elevated air pressure?

DR. HANNIBAL HAMLIN: Undoubtedly, there will be the same trouble with the term "blast concussion" as there was with "shell shock," used after World War I. The Navy could never be persuaded to use international nomenclature. The first thing one had to do in the Navy was to make a diagnosis, even before knowing anything about the patient. Blast injuries are not mysterious, but they do constitute a special group. They are comparable to what one sees in civilian life, as Dr. Denny-Brown has made clear in his experiments. The only mechanism that intrigues me is that of sudden compression under water. I am convinced that it does raise intracranial pressure to crucial levels. I am still in doubt as to whether or not it can cause petechial hemorrhages of the brain and death. I think it might. I do not know that this effect applies in airborne blast, and certainly not in solid blast. In Dr. Young's experiments the intracranial pressure remained elevated after release of bodily compression in a dog; the animal subsequently died, and autopsy showed petechial hemorrhages in the brain similar to those we have been discussing in human victims of blast. Moreover, dogs in which the jugular veins had been ligated exhibited no rise in intracranial pressure on bodily compression. The structures around the third ventricle and the hypothalamus might be affected seriously by rapid and tremendous rise in intracranial pressure. Otherwise, I see no difference between blast injuries and civilian injuries.

Dr. Schwab brought up the psychiatric effect of blast, which has been of more importance than organic injury. The patient Dr. White mentioned had both. I do not see how anyone could survive such an experience without psychologic trauma. More work will be done on this problem of blast because of its aftermath in veterans and its relation to the development of atomic energy.

I think that the mechanism in caisson disease is the same as that of blast injury except in terms of time. In submarine and aviation experience, change of pressure in either direction, if changed fast enough, can produce neurologic injury because the subject is not allowed to accommodate. Limits of tolerance are related to the degree of positive or negative pressure and to the time factor

Chronic Rheumatic Encephalitis. Dr. Clemens E. Benda, Wrentham, Mass.

While it is generally accepted that chorea minor is an acute manifestation of rheumatic fever and represents an exudative stage of cerebral involvement similar to the exudative changes which may be observed in the joints, heart and other organs, and which may heal without permanent damage, it is little known whether the exudative stage may turn into a chronic proliferative rheumatic disease of the brain. Chronic rheumatic manifestations are familiar in the heart (myocarditis and endocarditis), arteries (endarteritis), joints and other organs. Chronic rheumatic encephalitis is practically unknown. Bruetsch, of Indianapolis, emphasized in a series of publications the existence of chronic rheumatic encephalitis and maintained that in a certain percentage of cases a chronic rheumatic disease of the brain, with a variety of mental and neurologic manifestations, may be observed. In a comparative study of 200 brains of patients with a variety of symptoms of mental deficiency or deterioration, I encountered 2 brains in 1941 in which pathologic manifestations differed essentially from those of any other encephalitis or degenerative disease associated with other conditions. Comparison with Bruetsch's cases revealed the similarity of the pathologic pictures. Moreover, in both cases there were rheumatic heart disease and rheumatic endarteritis, and in 1 case a history of chorea could be obtained. With these observations the existence of chronic rheumatic encephalitis seems definitely established. The relation between the meningoencephalitis rheumatica and heart and joint disease seems somewhat similar to the relation between meningovascular syphilis and the primary and secondary infections of the body. Only a rather small percentage of persons have meningoencephalitis rheumatica. Not all these patients present striking symptoms referable to the heart or joints, and heart disease may develop insidiously and unnoticed in the course of many years. Certain predisposing factors in the involvement of the brain may be of possible significance. In further study of the material, 2 more cases were discovered in which similar lesions were present in the brain. In both cases, those of girls, there were striking neurologic manifestations, characterized by a chronic chorea and torsion dystony with conspicuous physical deformation. In additions to the common signs of chronic rheumatic encephalitis with scars in the cortex and endarteritis, there was severe involvement of the brain stem and cerebellum in both cases. The discovery that the puzzling manifestations of torsion dystony may be due to chronic rheumatic encephalitis throws new light on a possible etiologic factor in this condition and deserves further attention.

Dr. L. Raymond Morrison: It has been a great pleasure to hear Dr. Benda's paper on this important subject. For a long time I have hoped to see preparations of this sort, for the disease is well known and I have never happened to see a case myself. Clinically, it has been talked about since the last century. Trousseau recognized it from the psychiatric point of view. In the early part of this century people wrote about it, calling it cerebral rheumatism because during the course of acute rheumatic fever psychiatric disturbances occurred; afterward, the rheumatic fever apparently subsided but the mental symptoms persisted. It was not until recently that its pathologic basis was explained. There are a few points I should like to ask about. The first is perhaps merely a matter of terms. Dr. Benda spoke of Still's disease in relation to rheumatic encephalitis. As I understand it, Still's disease is rheumatoid arthritis, and not rheumatic fever. The pathologic processes are not similar. In the examination of a number of patients with rheumatoid arthritis, I have never found anything that resembled obliterative endarteritis in the brain or spinal cord. About the subcutaneous nodules of rheumatoid arthritis one sometimes sees obliterative endarteritis. I should like to ask whether Dr. Benda is convinced that the proliferation is of endothelial cells,

and not subendothelial connective tissue, for rheumatic fever in general is usually considered a disease of connective tissue, and the fibrinoid degeneration, which Dr Benda so well presented, is a widespread manifestation of this. According to the literature, most other investigators have not observed lesions in the basal ganglia. Dr. Benda should be congratulated as being among the first to demonstrate them. I believe that the presence of iron, also, is something new. I wonder if the case in which the iron was seen is of the same type as the others. Rheumatic encephalitis is apparently a disease much commoner than is realized. Kernohan, I believe, had 25 cases of rheumatic heart disease, and in 24 he found rheumatic encephalitis. I should like to say, again, how well I think this was done and how important I think it is.

DR. PAUL B. JOSSMANN: In this important paper, Dr. Benda has laid the ground for the concept of a pathologic entity. Yet he mentioned the scarcity of clinical observations, particularly in relation to the chronicity of the process in the central nervous system. I should like to refer briefly to observations on a group of 25 children who were studied in regard to a single neuropathologic symptom—tic. All these children had a history of Sydenham's chorea, and at shorter or longer intervals tics appeared, evidently of organic nature. Interest in the nature of tics was enhanced by experiences with tics in cases of chronic epidemic encephalitis. All tics which appeared in this group of children after chorea were of the "rheumatic" type. There was a comparatively large percentage of recurrent attacks of chorea—some of long duration, some chronic, some recurrent. Between attacks, the children presented tics of various muscles and muscle groups which could hardly be considered psychogenic. These tics in connection with, or as a result of, Sydenham's chorea reflect clinically the chronic process which Dr. Benda has outlined. In this connection I should like to ask him a few questions.

Some of the tics in epidemic encephalitis were studied anatomically. There were controversial opinions as to whether or not the hypothalamic region was involved. Has Dr. Benda seen lesions of the putamen, substantia nigra and caudate nucleus in his cases? In 1 of his 3 cases the posture reminded me of that in Wilson's disease. Did the localization of lesions suggest any anatomic similarity to Wilson's disease?

DR. LOUIS GOODMAN, Howard, R. I.: I appreciate the opportunity of hearing Dr. Benda's excellent paper and of commenting on it. I am convinced by his demonstration that the diagnosis of rheumatic encephalitis in his cases is valid.

However, I am in doubt about the specificity of the lesions which he describes. From Breutsch's report in 1940 of a 9 per cent incidence of rheumatic encephalitis in schizophrenic patients, it was my impression that he regarded the cerebral lesions as fairly specific. I should be interested to know what Dr. Benda's opinion is with regard to the question of specificity.

About a year ago Hassin reported 2 cases of toxic productive encephalitis (*J. Neuropath. & Exper. Neurol.* **4**:354, 1945), and I have since studied 2 similar cases. The lesions, although not so striking as the ones we have seen here, resembled them. There was no ascertainable etiologic factor in these cases, but Hassin stated that almost any infectious disease may produce such a pathologic change.

I should also like to comment on an even more striking similarity of the cerebral lesions of chronic hypertensive encephalopathy to those of rheumatic encephalitis. One may find a productive and proliferative endarteritis, focal areas of softening or gliosis, old and recent thromboarterial disease and focal perivascular ischemic lesions, all of which are described as characteristic of rheumatic encepha-

litis. It raises the question whether rheumatic fever may not also be responsible for the type of cerebral lesions accompanying chronic hypertensive encephalopathy, as well as rheumatic encephalitis. In that connection, therefore, I should be interested in learning whether Dr. Benda's patients showed an elevation of blood pressure.

DR. CLEMENT BENDA, Wrentham, Mass.: I thank Dr. Morrison for his creative criticism, which is very helpful. I agree with him that the comparison of chronic rheumatic encephalitis and rheumatoid arthritis is probably not entirely correct. Rheumatoid arthritis was mentioned by McCulloch as a chronic proliferative manifestation of rheumatic fever. It is also true that the endarteritic proliferations of the vessels are not of an endothelial character, but emphasis should be placed on the fact that they consist of subendothelial fibrous tissue.

I do not consider the iron deposits which were present in 2 cases of any specific significance, but it is interesting to remember that von Sántha described the brain of a child who died after an acute chorea of four weeks' duration (*Virchows Arch. f. path. Anat.* **287**:405, 1932). He demonstrated a vascular pathologic process identical with that observed by Dr. Bruetsch and me, but he mistook the occlusion of the vessels as thrombotic. He described well, however, the fibrinous exudation around the vessels and mentioned that the fibrin is mixed with iron pigments.

With regard to Dr. Jossman's question about the relation of cerebral localization and clinical symptoms, I did not go into more details because I felt that the lesions are so widespread that they would not permit any conclusion based on localization. It may be said, however, that in the first 2 cases, without chronic neurologic symptoms, the cortex was involved to a larger extent than the basal ganglia, whereas in the 2 cases with many involuntary movements the condition was reversed and the basal ganglia and cerebellum showed extensive pathologic change. As to the differential diagnosis of chronic rheumatic encephalitis and von Economo's (lethargic) encephalitis, the rheumatic type is characterized by extensive involvement of the pyramidal tracts, a Babinski sign and spasticity, in contrast to the extrapyramidal lesions of the latter type of encephalitis. By the way, in all the cases of Hallervorden-Spatz disease described in the literature there were a great deal of pyramidal involvement and pronounced resemblance to cases of torsion dystony.

Dr. Goodman discussed the question of specificity, which, of course, is an intriguing one. I feel that the full-fledged picture of rheumatic encephalitis is so characteristic that a diagnosis can be made on pathologic grounds, but many single lesions are usually not specific enough to make a definite differential diagnosis. It is true, however, that many eminent pathologists, such as von Glahn, Pappenheimer and MacCallum, have expressed the belief that the arterial changes in rheumatic fever are so specific that they can be distinguished from other lesions due to various noxious factors.

PHILADELPHIA PSYCHIATRIC SOCIETY

Samuel B. Hadden, M.D., *President, in the Chair*

Regular Meeting, Nov. 8, 1946

Introductory Question Period. As an innovation, the first fifteen minutes of each meeting of the society will be devoted to discussion from the floor of any questions of general interest to members of the society, especially problems related

to the practical aspects of psychiatric work. Among the questions raised, three have been selected.

1. *Procedure of hospitalizing a patient when the responsible relative is an ineffective person and the patient is unwilling to cooperate.*

DISCUSSION

Drs. M. F. Brody, S. B. Hadden, J. C. Yaskin and E. V. Eyman: 1. Formalities of admission must be completed. 2. The aid of several family members should be secured. 3. Deception should be avoided if possible, though some degree of subterfuge may at times be unavoidable. 4. Unless the patient is suicidal or dangerous, the family should be given adequate time to become convinced of the need of hospitalization in order to obviate premature removal of the patient.

2. *Local procedures for getting a dangerous patient to the hospital when the family is unable to handle the situation alone.*

DISCUSSION

Drs. L. H. Twyeffort, S. B. Hadden and A. M. Ornsteen: 1. Police cannot enter a home and remove a person unless charges have been preferred against him. 2. A member of the family may make contact with the police station and request police intervention. The member must express his willingness to go on record as having done so. 3. The police will then remove the patient to the city hospital, provided they have assurance that there is a vacancy. 4. However, if admission is to be a private institution, the police will not act. A constable and commitment papers will be required. Police will remove a dangerous patient to the police station and hold him until a police surgeon certifies the need of admission to a psychiatric hospital.

3. *Advisability of shock therapy (insulin or electric shock) for acute behavior problems of adolescence.*

DISCUSSION

Drs. M. K. Meyers, J. Rose, S. B. Hadden and J. C. Yaskin: 1. Rebellious behavior is merely a symptom occurring in many types of reaction. 2. Such drastic therapies as shock treatments are contraindicated without other justification.

Objective Tinnitus Aurium: Report of a Case with Recovery After Hypnosis. Dr. Manuel Pearson and Comdr. L. J. Barnes (MC), U. S. N. (by invitation).

Tinnitus is classified as the subjective and the objective type. The first, and most common, type, is heard only by the patient, whereas the objective type is heard also by an observer. The objective type is chiefly of vascular origin and is generally due to aneurysm or a vascular tumor. A second variety of objective tinnitus is muscular.

A review of the literature reveals a number of cases of the muscular type of objective tinnitus. The most accepted theory of its cause is that it represents a spasmodic contraction of the muscles about the opening of the eustachian tube. Several authors have noted the coincidence of a neurotic personality and objective tinnitus. No cases were reported with recovery.

A case was presented of a lieutenant in the Marine Corps who suffered from deafness, tinnitus and severe nervousness after the premature blast of a 5 inch gun during the Okinawa campaign. Five days later he noticed a peculiar clicking sound in his ears. He was transferred to several hospitals for diagnosis and

treatment. In February 1946 the nasopharyngoscopic examination revealed a rhythmic contraction of the tensor veli palatini, as well as of the soft palate. The tinnitus was considered to be a tic. Hypnosis was induced easily, and with strong suggestion the clicking sound disappeared and the patient had the first relief in eleven months. A personality evaluation revealed a mild disorder with a definite tendency toward tics and spasms. The patient was followed for six weeks, during which time he was free from audible tinnitus and his mood was considerably improved. The impression offered is that a tic developed as a result of the patient's habit of swallowing in order to clear his ears. This is the first case reported in the literature of recovery from the muscular type of objective tinnitus, and it strengthens the idea that the etiologic factor is functional.

DISCUSSION

LIEUT. (JG) E. A. THOMPSON, U.S.N.R.(W): The discussant read a prepared report on various statistical findings on the syndrome under discussion.

DR. A. M. ORNSTEEN: This case reminds me of that of a girl aged 18 whom I once saw. Any one can make this sound [the discussant leaned over, and the sound was confirmed by a member of the audience]. Laymen usually call it "clicking the bones of the ears." I do not believe this explanation; it is due, rather, to the contraction of the muscles that tense the eustachian orifices. This girl had had multiple complaints, including pain in the back of the neck, inability to relax, fatigue and irritability, as long as she could remember. She had received a variety of treatments and medications, without relief. Over the preceding five years her symptoms had become intensified and included what she referred to as a "creaking sensation at the nape of the neck, coming out of the right ear." Fearing that people would view her as insane, she had never mentioned this symptom to any one and refrained from sitting too close to people. Finally, she confided in her sister and allowed her to listen closely, and the objective actuality of the noise was confirmed. On examining this patient with a stethoscope, I could pick up a clicking noise at the nape of the neck and noted that it was also transmitted to the bones of the skull. A myogram ruled out the possibility of its being caused by tension of the muscles of the neck, and I concluded that it was due to a habit spasm based on the mechanism already mentioned.

DR. ROBERT A. MATTHEWS: During my internship my associates and I once observed objective tinnitus in a patient in the psychopathic ward. Her attending physician had first viewed the symptom as hallucinatory. Nevertheless, the patient defied us to listen closely to her ear. This we did, whereupon we discovered that the sound could be heard quite loudly. This woman had a tic of the soft palate. I remember another woman, a schizophrenic patient, who had a similar complaint, from which she recovered, although not from her schizophrenia.

I should like to report briefly a case of "subjective tinnitus" observed a few weeks ago at Jefferson Hospital. A middle-aged man experienced an annoying subjective tinnitus at a time when his wife was being treated for involutional depression with paranoid trends. In addition to the tinnitus, he suffered from an increasing depression; and, because it was reaching suicidal proportions, hospitalization was advised for electroshock therapy. After the third treatment the patient reported that the tinnitus was improved. After the fourth treatment he claimed that the tinnitus in the left ear had cleared entirely and that it had lost 90 per cent of its intensity in the right ear. After the sixth electroshock treatment a confusional state developed. The patient expressed paranoid ideas and heard

voices. The treatment was discontinued, and within a few days the confusion disappeared, without return of either the depression or the tinnitus. He returned to work two days later. My impression was that this rigid, insecure man had a prepsychotic, subparanoid personality, these trends being released by the organic changes incident to electroshock therapy. I have been wondering as to the exact nature of the tinnitus. Was it a psychosomatic manifestation of tension?

DR. A. S. TORNAY: I should like to call attention to the occasional experience that various persons may have had in noting a sort of "objective tinnitus" when descending rapidly in an elevator or when yawning a bit too loudly. These are examples of non-neurotic types of tinnitus.

DR. JOSEPH YAŞKIN: Tinnitus in the great majority of cases is not a psychosomatic manifestation. Usually it has a definite physical background. It may be caused occasionally by sclerosis, is present in many organic diseases of the ear and may even accompany certain forms of cerebral tumor.

COMDR. L. J. BARNES (MC), U. S. N.: We regretted very much losing Dr. Pearson from our staff when he left the service. His aid in bringing this perplexing case to a happy solution was most gratifying.

Sometime later we had another patient with a similar pharyngeal tic, presenting an audible tinnitus. On nasopharyngoscopic examination, the torus tubarius could be seen to rise. This was interpreted as the action of the levator palatini, and was in contrast to the condition in the previous case, in which the movement was of the lower inferior (membranous) portion of the eustachian tube, and was interpreted as the action of the tensor veli palatini. Hypnotherapy was successful in alleviating the tic in this case.

Major Neville Young reported a case of objective tinnitus (*Brit. M. J.* **1**: 414 March 28 1942 He summarized the current attitude toward the problem when he stated: "Fortunately this matter seems to be no more than of academic interest, and there is certainly no indication for any local treatment. The prognosis depends entirely on the psychological outlook."

The experience with these 2 patients amply demonstrates that something can be done simply, and with considerable benefit to the patient.

Psychiatric Diagnosis in Military Service. DR. MORRIS W. BRODY.

The present method of psychiatric diagnosis is unsatisfactory from a military viewpoint. The term psychoneurosis is often used erroneously in the Army, since war neurosis is not always a true neurosis. Other factors increase one's dissatisfaction with the terminology employed by Army psychiatrists. The soldier was stigmatized when psychoneurotic was the diagnosis and the resulting prejudice imposed difficulties when it became necessary to reassign him to a different unit. Popularization of the terms neurosis and psychoneurosis was harmful to the service, since soldiers used these words as a refuge behind which they might hide.

The Army Medical Corps recognized the problems arising from popularization of the concept of psychoneurosis and, as a result, prohibited the use of that term in forward areas, substituting the term exhaustion in its stead. Later in the war the use of the term psychoneurosis was prohibited in all medical installations, but reference to the particular type of neurosis, such as anxiety state or conversion hysteria, was retained. The use of all such terms as psychoneurosis, anxiety state and conversion hysteria serves no useful purpose in the Army, and their use should be discontinued.

A method of diagnosis was suggested for use in the military service. The diagnosis referred to a reaction type formulated as a brief running account of the

soldier's past, present and anticipated future effectiveness. Three brief case histories and their formulations were offered. A sample diagnosis would read as follows:

Reaction Type
Predisposition: Personality background excellent
Adjustment to military service: Excellent
External stress: Arduous combat for five months
Present reaction: Insomnia, tension, tremulousness, sensitivity to noise—moderate—improved
Effectiveness: Any type of duty in a noncombat area

DISCUSSION

Captain, M. C., A. U. S. (identity not established): My wearing the uniform makes me feel I have a responsibility to defend the psychiatric service.

I should like to make one point before I proceed to steal the doctor's thunder. The difficulty is not in the use of the term "psychoneurosis," but in the public stigmatization associated with it. No matter what term is used, if the public gets hold of it and uses it to stigmatize, that term will have a detrimental effect.

The problem, as I see it, is to educate the public to accept neuroses as illnesses, just as they have accepted other illnesses. One does not attempt to change the term "tuberculosis." That is not necessary, for, fortunately, there has been sufficient propaganda to educate the public into realizing that tuberculosis is not a disease which should be stigmatized. Furthermore, I should like to state that shortly after the term "psychoneurosis" was dropped by the Army a completely new classification was instituted. This classification has now been in use at least six to eight months, or perhaps longer. It was presented in *Technical Bulletin of Medicine 203.* This classification is essentially the same as that Dr. Brody suggested, though perhaps in slightly briefer form. No longer is there an "anxiety state"; the term is now "anxiety reaction." In place of "present reaction," "anxiety reaction" is used, followed by its manifestations, such as tremulousness, insomnia and tachycardia, denoting the patient's present reaction. As a subheading for the reaction types which the *Technical Bulletin of Medicine 203* has ordered Army psychiatrists to use, there is the term "external precipitating stress," referring to the amount of combat experience, and related factors. The next subheading, which has been used for some time, is "predisposition," as in Dr. Brody's suggested classification. A third subhead, that of "incapacitation," is also used, and under this heading merely the degree of incapacitation (mild, moderate or severe) is indicated.

I agree with Dr. Brody that this brief formulation is a useful adjunct in classification and in a better understanding of the patient at a glance. I should also like to make clear that commanding officers of line outfits never see charts of patients. These officers never get diagnoses, nor should they. In the service they are provided with a so-called profile number, which, by a numerical system, merely indicates the anticipated effectiveness of the patient. Incapacitations or limitations with regard to duty are specified and appear on the service record, but at no time does the line officer see a hospital chart.

DR. ALBERT KAPLAN: I should like to raise the question whether "war neuroses" are different from "peace neuroses."

DR. MORRIS BRODY: I am surprised to hear that the Army is now using essentially this type of diagnosis. I was not aware of it; surely, they were not using it in November 1945, at which time I left the service. I presented the material for my paper in April 1945, and it was sent to Washington through the regular channels. At that time one had to complete forms stating the diagnosis and duty status of the men one sent to the replacement centers.

I cannot fully agree with the captain regarding the education of the public. It is my feeling that, at least up to the present, much of the education the public has received has done more harm than good. This was brought home when it was attempted to teach the public how to treat the returning veteran, and it seemed only to stir up more anxiety than if they had not been given any education whatever. The press oversold the whole problem of psychoneurosis.

As to the question of a "war neurosis" not being the same as a "peacetime neurosis": The situation of war is an abnormal one, and that setting is not a guide to the person's ability to adjust or not to adjust. That is what I meant when I said that it is difficult to make the diagnosis of "psychoneurosis" under wartime conditions. I am convinced that in the military service the diagnosis of "psychoneurosis" was made too frequently. I believe that many persons designated psychoneurotic were not really psychoneurotic, but were given that diagnosis because they were unsuited to combat duty. In the Army, one could not say simply that the man was unsuited for combat duty. One had to make a diagnosis. If a man under combat exhibited certain symptoms, it meant merely that under that particular stress symptoms appeared, but many of these men, once they were reclassified and given duties similar to their peacetime activities, were relieved of all their symptoms. I cannot consider these symptoms as typical of peacetime neuroses.

DR. SAMUEL B. HADDEN: I differ with Dr. Brody's statement that this type of neurosis was not seen before the war. Comparable transient situations do occur in civilian life—witness the stock market crash of 1929, or those years when people stood on corners with boxes of apples. The threat of starvation to one's family and children can become an ever present nightmare and produce massive, acute anxieties. The civilian situation then was an extreme one, and extreme situations with the same type of threats do occur in civilian life. The neuroses have always been with us, which reminds me of the story of the grandfather who was asked by his grandson where he put his whiskers when he slept—inside or outside the covers. "Grandpop" didn't know; so that night he decided he would find out where he did put his whiskers. First, he left them on the outside of the covers, and that wasn't right. Then he stuffed them on the inside, and that wasn't right. In the same way, we have always had the neuroses with us, as the old gentleman always had his whiskers with him, and until the war, when we got all fussed up about the neuroses, we got along very well with them. I think we shall continue to do even better.

Short Term Hospitalization of the Alcoholic Patient. DR. C. NELSON DAVIS.

The management of 233 patients representing first admissions for alcoholism was reviewed. The patients were unselected and had the usual physical and mental complications of the alcoholic patient. After a five month period, 97 patients, or 41.6 per cent, were reported as "dry," whereas 136, or 58.3 per cent, were reported as "wet" or unaccounted for. This figure is encouraging and compares favorably with other published reports. However, exact statistics will be dependent on a long range study. The present preliminary report indicates merely a trend.

Attention was called to the usual long term hospitalization via commitment and its unhappy results, as well as to short term hospitalization against the patient's wishes and its equally poor results. The present practice of short term arrests by magistrates' courts again falls short of accomplishing its goal, if the goal is sobriety.

The present program of short term hospitalization, as carried out in the C. Dudley Saul Clinic is as follows: On admission the patient usually receives

1,000 cc. of a 5 per cent solution of dextrose in isotonic solution of sodium chloride, to which an ampule of "solu B" (a mixture of thiamine hydrochloride, 10 mg.; riboflavin, 10 mg.; pyridoxine hydrochloride, 5 mg.; calcium pantothenate, 50 mg., and nicotinamide, 250 mg.) and 10 units of insulin are added. Sedatives are administered for the first twelve to twenty-four hours, but sedation is restricted as far as possible. Many patients receive no sedation. No alcoholic beverage is given. Vitamins and tonic medications are given as indicated. Frequently, insulin, in a dose of 30 units, is given twenty minutes before meals.

All patients who are ambulatory attend daily group therapy sessions, in which talks are given by the attending physicians and by a patient with arrested alcoholism, followed by open discussion.

In addition, there is held a weekly open forum on alcoholism, designed primarily to acquaint the families and other interested persons, such as clergymen, social workers and nurses, with the nature of alcoholism, with what can be done to aid the alcoholic person and with the methods employed in the clinic.

The basic purposes of the work in the clinic are as follows: (1) to make the diagnosis of alcoholism and attendant complications, if any; (2) to provide the patient with a period of sobriety during which the exact nature of the disease can be explained to him; (3) to make it possible for him to accept his alcoholism and to make a decision to deal with it, and (4) to provide guidance for the patient in his adoption of a program for his life which will make it possible for him to live in sobriety.

Book Reviews

War Stress and Neurotic Illness. By Abram Kardiner, M.D. With the collaboration by H. Spiegel, M.D. Price $4.50. Pp. 428. New York: Paul B. Hoeber, Inc., 1947.

This book gives a timely analysis of a problem of interest to many psychiatrists, that of traumatic neurosis, and offers suggestions in the handling of this problem. In the section on battle psychiatry, the author proposes to solve the conflict (between duty and self preservation) of the soldier on the field, utilizing the concept that the acute stage of the neurosis is a physioneurosis and that, after the acute stage, the neurosis is tightly bound to the pretraumatic personality.

He finds that the traumatic experience may precipitate any of the well known neuroses or psychoses, but indicates that there is something distinctive about traumatically precipitated neuroses. Most characteristic is the "threat of annihilation" and the patient's continued attempts to adapt himself to this threat with depleted resources. At this point the mechanism of "secondary gain" (escape from combat compensation) comes into play to complicate the picture further.

Dr. Kardiner further indicates that the libido theory does not suffice to explain the pathology of the traumatic neurosis. He supplants the operational instinct, a conative principle, with the "action" system, a morphologic principle. On the whole, the author feels that the theoretic concept of traumatic neurosis is reconcilable with that of the general theory of neuroses.

Particularly interesting and significant are Dr. Kardiner's comments on the role of adaptation in this illness, and his discussions of the dream life and the epileptic symptom complex may be considered highlights of the book. This is an important contribution to understanding of the basic concepts of psychopathology. It is presented in a clear and concise manner and is fortified throughout with excellent case material. The book is highly recommended.

Place of Psychology in an Ideal University. Report of the University Commission to Advise on the Future of Psychology at Harvard. Price $1.50. Pp. 42. Cambridge, Mass.: Harvard University Press, 1947.

This book, of forty-two pages, is the report of the University Commission to Advise on the Future of Psychology at Harvard. The men on the commission were eminent and represented many fields. The chairman was Alan Gregg, and the members were Drs. Barnard, Bronk, Carmichael, Dollard, French, Hilgard, Hunter, Thorndike, Thurstone, Whitehorn and Yerkes. The commission was appointed in May 1945 and worked until early 1947. The report is brief, meaty and important. In the deft turn of phrase one recognizes the writing of the chairman.

The summary is best put in the commission's own words:

"We present the following summary of what we believe to be the more important aspects of this report.

"We have defined psychology and discussed its trends and its range. All the evidence indicates that it is young, growing, extending especially in the direction of social psychology, and tending toward applied or clinical forms. Psychology exerts a marked interest for undergraduate students and has likewise come to

occupy a very important place in the public's estimation and expectations. Its potentialities as a part of the training of the undergraduate student are considerable, but probably the greatest contribution psychology can make is to education as a whole—partly by drawing attention to the value of reckoning with the nature of the recipient of education, partly by using what is already known regarding the learning process.

"The major contributions of psychology to the university are in the general orientation afforded by introductory courses, the advanced training for special degrees, and the still unbounded contributions to be secured through research. The value of the other courses available in the university to the student of psychology are more than equalled by the contributions of psychology to the other departments of the university and especially to its professional schools.

"We recommend as axioms of policy that psychology be given opportunity and freedom for change and development, that all the psychologists in the university be brought into contact with each other in an effectual and continuing way, that the department be large enough and well enough supported to interest and reward a large variety of psychologists, and that the time is at hand for the creation of a course to train clinical psychologists (psychotechnologists).

"We do not regard the separation of clinical and social psychology from all the rest of psychology, or a concentration in certain directions, as a gain in unity for the field as a whole. We believe that arrangements which encourage the exclusive domination of psychology by the laboratory would sacrifice the unity of the subject, belie its freedom, and limit its opportunity.

"An extraordinary opportunity exists for an ideal university to realize the potentialities of psychological research, of introductory and advanced teaching of increasing numbers of students, and in the training of practitioners of psychology to meet an increasing demand. For this demand transcends in importance the discomforts of psychology's growing pains."

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